

A contemporary history of the origins and development of UK Biobank 1998-2005

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## **Abstract**

### Background

This thesis examines the origins and early development of UK Biobank. This is a resource funded in 2002 by the Medical Research Council, the Wellcome Trust, the Department of Health and the Scottish Executive to gather genetic and lifestyle information from half a million participants aged 40-69 years old in the UK and monitor their health for up to thirty years in order to improve the prevention, diagnosis and treatment of major diseases. UK Biobank was set up following the completion of the Human Genome Project in 2001, and was one of many established at around the same time with the goal of translating the knowledge of the human genome sequence into practical benefits for human health. (National genetic databases were also set up or proposed in Iceland, Estonia, Latvia, Sweden, Singapore, Tonga, Spain, and the United States). They, and the Human Genome Project, had raised a number of important issues about access to and ownership of genetic information.

### Aims

The original aim of my PhD was to examine lay and professional understandings and responses to Biobank in the light of this background. However, UK Biobank took longer than expected to reach the stage of data collection, in part because of negotiations about its organisational structure. The aim therefore changed to address the question of how and why was UK Biobank initially configured in the manner it was.

### Organisational structure

UK Biobank was originally set up by the funders with a ‘hub’ and ‘spoke’ model, with calls for bids from UK Universities for a central ‘hub’ charged with financial management and overall control of data and samples, and ‘spokes’ who were responsible for recruitment and data collection through primary care. The selection of both was made through the procurement rules of the EU. The hub (Manchester), six regional spokes, and the CEO (from Oxford) were all appointed simultaneously in 2003 and subsequently a Board of Directors and a number of committees were appointed. The CEO resigned in late 2004, and a new CEO and Principal Investigator

was appointed in 2005, after which there were significant changes to the organisational structure.

### Methods

I conducted 76 oral history interviews with academic scientists directly and indirectly involved in UK Biobank, representatives of all four funding bodies, and representatives of UK Biobank Limited (the company set up to manage UK Biobank). I also conducted archival analysis of the MRC's official documents concerning the origins and development of UK Biobank.

### Findings

From its beginning UK Biobank was marked by tension between academic scientists on the one hand and representatives of the funding bodies and UK Biobank Limited on the other. Academic scientists criticised the funding bodies for establishing UK Biobank in a way that departed from what I have termed 'standard academic scientific practice'. Spokes felt they should receive some privileged access to data they would contribute to collecting, and felt that the set up did not recognise the performance indicators driving scientists and universities. Lack of clarity over who was in control of UK Biobank contributed to these tensions as both spokes and funders felt that the other exerted undue influence. Some mistrust developed between academic scientists and representatives of the funding bodies and UK Biobank Limited.

### Discussion

The configuration of UK Biobank was difficult for academic scientists and representatives of both the funding bodies and UK Biobank alike. Organisational issues, typical of those confronting Big Science initiatives, were largely responsible for this difficult legacy. Issues of leadership, the hub and spoke model, the sequencing of funding decisions, appointment of groups and committees and protocol development, uncertainties about who was in control, and ambiguities within the organisational structure as a whole were the most significant issues in the origins and development of UK Biobank, as the organisational changes in 2005 testify.

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## **Preface**

### *Background to my PhD studentship*

In May 2003 Professor Sally Macintyre and Professor Kate Hunt at the MRC Social and Public Health Sciences Unit<sup>1</sup> at the University of Glasgow advertised a PhD Studentship on ‘Lay and professionals’ experiences and views of the MRC/Wellcome Biobank Project’. The topic reflected their research interests and that of the Unit, and emerged from the Unit’s long standing interest in public engagement with science, particularly epidemiological science. MRC Head Office was not involved in the selection of the topic nor did they have any role in approving the title.

I was a Wellcome Trust funded masters’ student at the Centre for the History of Medicine also at the University of Glasgow,<sup>2</sup> completing my MPhil in the History of Medicine in 2003, including a dissertation topic on ‘Infanticide in Scotland, 1830-1840’ using justiciary court records from the National Archives of Scotland and doctors’ tracts of the period as sources.

My application for the PhD Studentship at the MRC Social and Public Health Sciences Unit supervised by Professor Sally Macintyre and Professor Kate Hunt was successful. Once I took up the studentship, my supervisors and I changed the title to ‘A contemporary history of the origins and development of UK Biobank’ to reflect my background as a medical historian and in response to factors relating to UK Biobank itself: by September 2003 UK Biobank’s implementation was delayed making it impossible to examine perceptions of the endeavour. This shift of focus prompted us to seek a co-supervisor with a historical background. We contacted the

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<sup>1</sup> The MRC Social and Public Health Sciences Unit (MRC SPSU) receives core funding from the UK MRC and the Chief Scientist Office at the Scottish Executive Health Department. It is located at the University of Glasgow and is an affiliated member of the University’s Division of Community Based Sciences. It aims to ‘promote human health via the study of social and environmental influences on health’ (<http://www.msoc-mrc.gla.ac.uk> 2007) (accessed 16/02/07).

<sup>2</sup> The Centre for the History of Medicine was established in the University of Glasgow in 1985. It is now part of the Department of Economic and Social History and a member of the School of Historical Studies. Its research interests and activities cover the history of medicine from the early modern period to the twentieth century (<http://www.gla.ac.uk/History/Medicine/about%20the%20centre.html> 2007) (accessed 16/02/07).

Centre for the History of Medicine at the University of Glasgow, and Dr. Marguerite Dupree agreed to be a third supervisor.

### *Background to UK Biobank*

The Human Genome Project (HGP) was a crucial antecedent to UK Biobank, and paved the way for research into the role of genes and lifestyle factors in the development of disease. The HGP, an international effort to map<sup>3</sup> and sequence<sup>4</sup> the human genome, took place between the mid-1980s and the first few years of the twenty-first century. Completion of the first draft of the human genome in 2001 heralded the beginning of the ‘post-genome challenge’, which was seen by some scientists as an opportunity to utilise the knowledge gained from the HGP to create practical benefits for human health, for example through improved drug treatments and personalised medicine.

UK Biobank originated as an endeavour to construct a national database of health and lifestyle data, and blood and urine samples, from half a million healthy volunteers aged between 40 and 69 years old. It was borne out of the opportunities presented by the HGP, and is an example of one response to the ‘post-genome challenge’. UK Biobank was funded by the Medical Research Council (MRC),<sup>5</sup> the Wellcome Trust,<sup>6</sup> the Department of Health (DoH),<sup>7</sup> and the Scottish Executive.<sup>8</sup> It officially began with

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<sup>3</sup> Determination of the relative positions of genes on a DNA molecule (chromosome or plasmid) and of the distance, in linkage units or physical units, between them (<http://www.doegenomes.org> 2007) (accessed 16/02/07).

<sup>4</sup> Determination of the order of nucleotides (base sequences) in a DNA or RNA molecule or the order of amino acids in a protein (<http://www.doegenomes.org> 2007) (accessed 16/02/07).

<sup>5</sup> The MRC is a national organisation established in 1913 and funded by the government through an annual Grant from parliament via the Office of Science and Technology (OST), part of the Department of Trade and Industry (DTI). It promotes research into all areas of medical and related science with the aims of ‘improving the health and quality of life of the UK public and contributing to the wealth of the nation’. It is an independent organisation regarding the types of research it decides to support but works closely with Health Departments, Research Councils, industry and others in identifying and reacting to current and future health needs (<http://www.mrc.ac.uk/index/about.html> 2006) (accessed 14/02/06)

<sup>6</sup> The Wellcome Trust is an independent charity established in 1936 to fund research to improve human and animal health. It is the largest non-governmental source of funds for biomedical research in the UK and is privately endowed, thus independent from governments, industry and donors. It was founded by Sir Henry Wellcome who established a pharmaceutical company and, when he died, this charity (<http://www.wellcome.ac.uk/aboutus> 2006) (accessed 14/02/06).

<sup>7</sup> The Department of Health aims to ‘improve the health and wellbeing of people in England’ (<http://www.dh.gov.uk/AboutUs/fs.en> 2006) (accessed 14/02/06). It is not responsible for the running of the NHS or social services but instead works with health and social care organisations, arm’s length bodies and public and private sector organisations in delivery of health and social care. It is accountable to the public and government for the overall performance of the NHS, personal social services and the operation of the Department. Its ministers are led by the Secretary of State and

the formal commitment of funds in 2002. The MRC<sup>9</sup> and the Wellcome Trust<sup>10</sup> also funded a number of case-control studies following a call for proposals in 2000 in response to the ‘post-genome challenge’.

UK Biobank was just one example of a national genetics database established in response to the ‘post-challenge challenge’. A further national genetics database was planned in Britain in response to the post-genome challenge: Generation Scotland was proposed in 1999 and received initial funding from the Scottish Executive in 2003.<sup>11</sup> National genetic databases were set up or proposed in a number of countries across the world, including Iceland, Estonia, Latvia, Sweden, Singapore, Tonga, Spain and the United States. UK Biobank was therefore part of an international set of studies, which took place in the late nineteen-nineties. These proposals used the ‘post-genome challenge’ language of a ‘new era in medicine’ and ‘personalised treatment’. The international context of genetic database proposals added a further dimension to such expressions and infused them with greater potency. It is the aim of this thesis to provide a contemporary historical account of this one British response to the ‘post-genome challenge’.

### *Acknowledgements*

I would like to take this opportunity to thank the interviewees who took part in my study and the individuals at MRC Head Office who facilitated my access to MRC documents on the origins and development of UK Biobank. I am very grateful to all of the interviewees for their interest in my research and their generosity with their time, without which my study would have been impossible. Archival research of the MRC documents was an invaluable asset to my research and I would like to thank the Head of Corporate Affairs, Jane Lee, who permitted my access to these documents. I would also like to thank Wendy Raymond (MRC Corporate Affairs) for her practical

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appointed by the Prime Minister and are responsible for taking health and social care policy forward. (<http://www.dh.gov.uk/aboutus/howdhworke/dhobjectives/fs/en> 2006) (accessed 14/02/06).

<sup>8</sup> The Scottish Executive is the devolved government for Scotland (<http://www.scotland.gov.uk/About> 2007) (accessed 16/02/07).

<sup>9</sup> Following a successful bid for additional funds to develop new DNA collections, including UK Biobank, in the 1998 Government Comprehensive Spending Review (see chapter 3).

<sup>10</sup> Through their Functional Genomics Development Initiative ([http://www.wellcome.ac.uk/doc\\_WTD003288.html](http://www.wellcome.ac.uk/doc_WTD003288.html) 2006) (accessed 14/02/06)

<sup>11</sup> Generation Scotland involves two major studies, the Scottish Family Health Study (GS: SFHS) and Genetic Health in the 21<sup>st</sup> Century (GS: 21CGH) and was officially launched in February 2006 (<http://129.215.140.49/gs/gabout.html> 2006) (accessed 14/02/06)

support and friendliness. Wendy organised all of my visits to Head Office throughout my research (arranging desk space for me in a busy office) and always made me feel very welcome, which made my frequent trips to London far easier.

I would especially like to thank Sally Macintyre, Kate Hunt and Marguerite Dupree for their excellent supervision throughout this project. Their constant support, encouragement and critical suggestions ultimately made this thesis possible. I am particularly grateful for their continuous enthusiasm toward my research, which was a great source of motivation. I would also like to thank Malcolm Nicolson for reading and commenting on a draft of this thesis. My parents, Catherine and Patrick Langan, have continued to support and reassure me throughout my studies for which I am very grateful. Finally, considerable thanks go to Douglas Aiton for going through this experience with me and sharing in all the highs and lows.

### **Abbreviations**

ALSPAC – Avon Longitudinal Study of Parents and Children

APBI – Association of the British Pharmaceutical Industry

BDA – British Diabetic Association

BHF – British Heart Foundation

BIA – Bio-Industries Association

BoD – Board of Directors

BSA – British Sociological Association

CCC – Central Co-ordinating Centre

CEO – Chief Executive Officer

CERN – Centre Européen de Recherche Nucléaire

CMO – Chief Medical Officer

CRC - Cancer Research Campaign

DOE – Department of Energy

DoH – Department of Health

EGC – Ethics and Governance Council

EGF – Ethics and Governance Framework

EPIC – European Prospective Investigation of Cancer

ESA – European Space Agency

ESRC – Economic and Social Research Council

EST – Expressed Sequence Tag

EWG – Expert Working Group

GGPR – Genealogy Genotype Phenotype Resource

GIG – Genetics Interest Group

GPRF – General Practice Research Framework

HGC – Human Genetics Commission

HGP – Human Genome Project

HOPB – Head Office Project Board

HSD – Health Sector Database

IAG – Interim Advisory Group

IBIG – Inter Board Initiatives Group

ICRF – Imperial Cancer Research Fund  
IMA – Icelandic Medical Association  
IP – Intellectual Property  
IPC – Intensively Phenotyped Cohort  
ITN – Invitation to Negotiate  
JFAT – Joint Funders Action Team  
JVA – Joint Venture Agreement  
LMB – Laboratory of Molecular Biology  
MRC – Medical Research Council  
MRCT – Medical Research Council Technology  
MREC – Multi-centre Research Ethics Committee  
NIBSC – National Institute for Biological Standards and Control  
NIH – National Institutes of Health  
NoCTEN – North Thames GP Research Network  
ONS – Office of National Statistics  
PDC – Protocol Development Committee  
PI – Principal Investigator  
PQQ – Pre-Qualifying Questionnaire  
PSP – People Science and Policy  
RAE – Research Assessment Exercise  
RCC – Regional Collaborating Centre  
SOP – Standard Operating Procedure  
SSK – Sociology of Scientific Knowledge  
STOPAT – Space Telescope Observatory Performance and Assessment Team  
SWOT – Strengths Weaknesses Opportunities Threats

**Declaration**

This thesis has been composed entirely by myself, and the work in which it is based is my own.

Mairi A. Langan



## **Chapter 1**

### **Introduction and Literature Review**

#### **1.1 Background and Aim**

##### **1.1.1 ‘The UK Biobank gets funding go-ahead’**

Funding for the world's largest study of the role of nature and nurture in health and disease was announced today ... the study will capitalise on the knowledge from the Human Genome Project ... The combination of volunteers' genetic, medical and lifestyle information will position the biobank study as a powerful resource to help researchers unravel the origins of ... important diseases ([http://www.wellcome.ac.uk/doc\\_WTD002895.html](http://www.wellcome.ac.uk/doc_WTD002895.html) 2002) (accessed 19/12/06).

This press release issued on the 29 April 2002 announced the joint decision of the MRC, Wellcome Trust and the DoH to fund UK Biobank, and heralded the official beginning of the endeavour. The announcement followed several years of planning by the MRC and Wellcome Trust, which formally began with an official meeting between them in May 1999. The press release illustrates the significance of the ‘post-genome challenge’ for the development of UK Biobank by positioning it as a response to the opportunities presented by the HGP. It points to the potential benefits to human health to be gained from utilising the knowledge from the HGP, specifically in assessing the role of genes and lifestyle in the development of disease. It also demonstrates the international context of genetic databases by describing UK Biobank as the ‘world’s largest’.

The funding bodies’ comments that accompanied this press release reinforced the position of UK Biobank as a response to the ‘post-genome challenge’. The then leaders of the MRC and Wellcome Trust, Sir George Radda and Dr Mike Dexter, justified UK Biobank in terms of its ability to capitalise on the opportunities presented by the HGP. For example, Dr Dexter remarked that ‘[t]he UK biobank is a natural progression of the Wellcome Trust's involvement in the Human Genome Project’, and Sir George Radda commented that ‘[t]his exciting project may one day herald a new

era of medicine. In 20 years time, we may see individualised approaches to disease prevention and treatment' ([http://www.wellcome.ac.uk/doc\\_WTD002895.html](http://www.wellcome.ac.uk/doc_WTD002895.html) 2002) (accessed 19/12/06). The then Minister of Health, Lord Hunt, commenting on behalf of the DoH, focussed on the international context of genetic databases: 'The UK is leading the world with this exciting project ... It under-scores the Government's current investment for a better patient-focused health service' ([http://www.wellcome.ac.uk/doc\\_WTD002895.html](http://www.wellcome.ac.uk/doc_WTD002895.html) 2002) (accessed 19/12/06). The funding bodies' comments reflect a common theme associated with the promise of the 'post-genome challenge', that of personalised healthcare where drugs and treatment are tailored toward a particular person's constitution.

### 1.1.2 The 'post-genome challenge' and UK Biobank

UK Biobank emerged amidst a climate of great promise regarding the opportunities presented by the HGP to improve human health. For example, the then Chief Executive Officer (CEO) of UK Biobank Limited, John Newton, commented in a speech at a Parliamentary event in April 2003:

the last few years of the last century saw biomedical science transformed by the Human Genome Project. The new genetics provides a stunning opportunity to move ahead in our understanding of variability in human health ([http://www.wellcome.ac.uk\\_WTD002871.html](http://www.wellcome.ac.uk_WTD002871.html) 2003) (accessed 16/02/07).

The HGP not only presented new opportunities for gene research but opened up new avenues for the whole of biological research. Such was the promise that the HGP was seen to represent that it was described as the 'Holy Grail of biological science' (Glasner 2002) (p. 267). Similarly John Sulston (leader of the UK part of the HGP) described it as 'a work of reference as indispensable to biologists as a dictionary to a writer' (Sulston and Ferry 2002) (p. 247). Much of the excitement surrounding the mapping and sequencing of the human genome was attributed to its association with 'Big Science' (Glasner 2002). The HGP represented biologists' first claim to Big Science, previously the reserve of physical scientists. Scientists responded to the 'post-genome challenge' by developing ways to transform the abstract knowledge collected in the HGP into practical benefits for healthcare, thus justifying the Project. It set scientists 'scrambling to develop new techniques that exploit genome data to ask

entirely new questions' (Glasner 2002) (p.269). The way in which UK Biobank was announced stressed that it would use the knowledge gained from the HGP to explore the role of genes and lifestyle factors in the development of disease.

Funding bodies played a decisive role in getting both the HGP and UK Biobank underway. In the HGP, the United States group (the largest group involved) was led by the National Institutes of Health<sup>12</sup> (NIH) and the Department of Energy<sup>13</sup> (DOE), and the UK effort was funded by the Wellcome Trust and the MRC. The HGP, like UK Biobank, was a collaborative venture and brought scientists, social scientists and funding bodies together nationally and internationally. The effort to map and sequence the human genome also included groups from France, Italy, Germany and Japan. I will examine the origins and development of the HGP in detail later in this chapter. The significant involvement of funding bodies and collaboration between different groups of researchers are characteristic of Big Science. I will explore the concept of Big Science and the origins and development of Big Science projects in the literature review below.

### 1.1.3 Why a contemporary history?

Considerable optimism surrounded the promise of the 'post-genome challenge' to improve human health. Biologists spoke of dramatic changes in healthcare that would be wrought by the completion of the human genome map and the opportunity to utilise the information gained for practical benefit. UK Biobank was a product of this promise and the funding bodies utilised the language associated with the 'post-genome challenge' to support it. They stressed UK Biobank's potential to initiate powerful changes in disease prevention, treatment, and the practice of medicine in the twenty-first century. UK Biobank's emergence amidst this excitement renders it an important subject for study. National genetic databases were a relatively common

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<sup>12</sup>The National Institutes of Health (NIH), a part of the U.S. Department of Health and Human Services, is the 'primary Federal agency for conducting and supporting medical research' (<http://nih.gov/about> 2007) (accessed 16/02/07).

<sup>13</sup>The U.S. Department of Energy (DOE) is a national security agency that develops innovations in science and technology as one of its missions (<http://www.energy.gov/organization/index.html> 2007) (accessed 16/02/07).

response to the completion of the HGP and resources were allocated for these across the world, including Iceland, Estonia, Latvia, Sweden, Singapore, Tonga, Spain and the United States (Austin, Harding et al. 2003). Advocates of national genetic databases stressed their potential to transform healthcare through personalised medicine.<sup>14</sup> Given the potential benefits predicted to flow from such national genetic databases, my study of the origins and development of UK Biobank, a leading example of the field, is particularly timely.

#### 1.1.4 Aim

The aim of my thesis is to document and analyse the origins and development of UK Biobank in its contemporary historical context. I define ‘origins’ here as the period from the first official meetings within the MRC during 1998 that led to the first official joint meeting between the MRC and the Wellcome Trust in 1999 regarding what became UK Biobank, through formation of the initial protocol and up to the funding decision in April 2002. By ‘development’ I mean the period from the funding decision, through implementation of the original organisational structure, until key organisational changes occurred in August 2005. I chose the funding decision as representative of the change from ‘origins’ to ‘development’ as it signalled the funding bodies’ formal commitment to UK Biobank, and allowed implementation of an organisational structure. I have investigated the origins and development of UK Biobank from its inception in 1998 until the organisational changes in August 2005.

The original research question was: how and why was UK Biobank established at this time and in this manner? I intended to examine the particular ways in which the idea for UK Biobank emerged, when and from whom. I sought to explore explanations for the establishment of a national genetics database in the UK. However, the focus of my research shifted following the first period of fieldwork. Interviewees tended to focus on the practical set up of the UK Biobank, rather than the origins of the idea itself, which they largely ignored. Therefore following initial interviews, the research

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<sup>14</sup>For further discussion of the international context of national genetic database proposals see: (Berger 1999), (Chadwick 1999), (Metspalu 2002), (Merz, McGee et al. 2004), (Bosch 2004), (Burton 2002), (Burton 2002)

question focussed more on how and why UK Biobank was configured the way it was, and less on how and why the concept of UK Biobank originated.

UK Biobank was formally established with the funding decision in April 2002. I began my study of its origins and development in October 2003, just one and a half years later. I therefore had the opportunity to witness the development of this new scientific endeavour as it went through the initial period of development. Conducting research into the origins and development of UK Biobank at this early stage had advantages and disadvantages. The merits of conducting such contemporary history will be addressed in chapter three.

UK Biobank underwent significant changes during the period of my research both in terms of scientific design and organisational structure. This evolving nature strongly influenced the development of my research and accounted for a further change to the title of the PhD. UK Biobank had planned to have begun recruiting participants prior to the commencement of my PhD, but it had not developed to that extent when my research began in October 2003 nor indeed several years later. UK Biobank had not therefore developed sufficiently to allow analysis of its implementation within the time frame of my PhD research. Therefore, the title of the thesis changed from ‘A contemporary history of UK Biobank’ to ‘A contemporary history of the origins and development of UK Biobank’.

The focus of my research is on organisational aspects of the establishment of UK Biobank rather than the scientific merits of its design. My lack of scientific training and the evolving nature of UK Biobank (the protocol was still not finalised at the completion of fieldwork) would have made a scientific evaluation of UK Biobank difficult. Instead, I focus on organisational issues; for example, I investigated explanations for the particular organisational model chosen rather than justifications for the sample size, age range or prospective design. Scientific issues were considered, but only insofar as they illustrated themes in the origins and development of the resource.

My research was exploratory in nature and was not undertaken in response to a particular problem defined in the literature. I did not therefore research the origins and

development of UK Biobank with a hypothesis in mind, rather analysis of the literature served to inform the exploration. Since national genetic databases were a new and evolving phenomenon there was not a considerable body of research on them when I started my study.

## 1.2 Description of the Human Genome Project

### *Origins*

The HGP was an international effort to map and sequence the human genome. It started in the mid-1980s and was completed in February 2001 with the publication of a working draft of the human genome sequence (Glasner 2002). The largest group in the HGP was from the United States, led by the NIH and the DOE. James Watson (co-discoverer of the structure of DNA) initially led the US effort from 1988 to 1996 and was replaced by Francis Collins (Cook-Deegan 1994). The second-largest group was from the UK, led by Sir John Sulston of the Sanger Centre (the largest genome sequencing centre outside the US), and was largely funded by the Wellcome Trust, but also by the MRC.

The potential of biology to be ‘Big Science’ inspired the molecular biologist and chancellor at the University of California, Robert Sinsheimer, to try to set up an Institute to Sequence the Human Genome at Santa Cruz in 1984. The idea occurred to him after a failed attempt to secure a contract to build an astronomical telescope at his facility (Wilkie 1993). Sinsheimer organised a meeting of America’s leading molecular biologists in May 1985 to discuss the idea. Their reaction was however negative and doubts were raised over the ability of such a project to yield enough knowledge to justify the cost and magnitude (Roberts 2001). An Institute to Sequence the Human Genome was never established but the idea remained. Independently, similar ideas were taking shape in other research laboratories. For example, in 1985 the Nobel prize winning molecular biologist, Renato Dulbecco, gave a speech on the possibility of mapping the human genome and published extensively on the subject (Cook-Deegan 1994). The US DOE was also involved in proposals for a HGP. Its involvement developed from advances in nuclear technology and attempts to understand the effects of radiation on humans and their genes (Wilkie 1993). The Director of the Office of Health and Environmental Research at the DOE, Charles DeLisi, was inspired by a report from the 1984 Alta Summit (sponsored by the DOE and the International Commission for Protection against Environmental Mutagens and Carcinogens to discuss the ability of new DNA analytical methods to detect mutations) to propose the idea for a human genome project (Cook-Deegan 1989). In 1986 the DOE supported his plans to sequence the human genome at a meeting in

Santa Fe. The costs of such an endeavour, declared prohibitively expensive by the group at Santa Cruz, were manageable with the DOE's extensive budget (Wilkie 1993).

The origins of the HGP in the United States were marked by tension between the NIH and the DOE. Many molecular biologists looked toward the NIH for leadership as it funded most biomedical research. Biologists were comfortable with the NIH peer-review system and questioned DOE involvement. For example, David Botstein (a genetic mapper at the Massachusetts Institute of Technology) criticised DOE proposals as 'a scheme for unemployed bombmakers' (Roberts 2001) (p.1184). James Wyngaarden (head of NIH at the time) described the DOE's efforts as 'like the National Bureau of Standards proposing to build the B-2 bomber' (Cook-Deegan 1994) (p.139). However, the NIH was not initially as committed to the Project as the DOE. For example, in October 1986 the NIH Director's Advisory Committee concluded that the NIH should avoid Big Science (Cook-Deegan 1994). Some molecular biologists feared that if the NIH funded the Project it would be detrimental to the funding of other research activities. The Project was also criticised on the grounds that it was contrary to the traditional way biology was practised, a large co-operative effort as opposed to small scale individual led studies (Roberts 2001). Similarly the Project departed from the accepted notion that the best biological practice ensued from hypothesis driven research (Collins, Green et al. 2003). An advisory panel to the DOE in 1987 suggested that it take control of the Project because the DOE was more suited to hosting large scale scientific studies than the NIH (Roberts 2001). However, following the departure of DeLisi (their biggest advocate of genome research) from his position as Director of health and environmental research in December 1987, the DOE's involvement in the HGP diminished (Cook-Deegan 1994).

On October 1 1988, the NIH and the DOE signed a memorandum of understanding regarding the co-operation of the two agencies over genome research (Cook-Deegan 1994). This heralded the beginning of the US HGP, under the control of the NIH as opposed to the DOE. The appointment of James Watson as Associate Director for Human Genome Research, also on October 1 1988, lent the project considerable credibility. In 1989, the Project became independent of the National Institute for



General Medical Sciences and moved into the National Center for Human Genome Research and controlled its own budget. By 1989 the budget had increased to almost \$60 million (double the DOE allocation of \$28 million). By 1991 it reached \$108 million compared to the DOE's \$46 million budget, which further cemented the NIH's control of the Project (Wilkie 1993).

Research into Ethical, Legal and Social Issues (ELSI) began in the early stages of HGP in October 1989. The American ELSI programme was funded with 3-5% of NIH HGP funds and began with a broad scope. Its first announcement included five general questions:

What are the concerns to society and to individuals arising from the HGP?  
What specific questions in the broad areas of ethics and law need to be addressed? What can we learn from precedents? What are the possible policy alternatives and the pros and cons of each? How can we inform and involve the public and stimulate broad discussion? (Cook-Deegan 1994) (p. 239).

The UK was involved from the beginning in debates about a co-ordinated HGP. For example, John Sulston represented the Laboratory of Molecular Biology in Cambridge (LMB) at the Santa Cruz meeting (the first meeting held on human genome sequencing at the University of California) in 1985 and Sydney Brenner (Director of the LMB) had a seat on the National Academy of Science panel that constructed the framework for the HGP. In 1986 Sydney Brenner began the UK genome project with his own private funds until the UK Department for Education and Science awarded an £11 million grant to the MRC to fund the project in 1989. By 1992, the budget was £5.9 million per year, and when combined with other grants from within the MRC, the total was £20 million (Wilkie 1993). In 1994, the Sanger Centre was built with a grant of £40-£50 million from the Wellcome Trust, alongside the new European Bioinformatics Unit and the relocated Human Genome Mapping Project Resource Centre, to begin work on the HGP at Hinxton, Cambridge. In May 1997, following a successful application to the Wellcome Trust, the Sanger Centre's funding was doubled to complete a third of the human genome (Sulston and Ferry 2002).

### *Development*

Controversial issues accompanied the development of the HGP. In the United States in 1991, the NIH applied for patents on several hundred fragments of genes called Expressed Sequence Tags (ESTs). It claimed the right to the ESTs, the genes that they represented and the proteins encoded by these genes. This move reflected the wish of Bernadine Healy (the then head of the NIH) to advance the commercial development of scientific discoveries. James Watson criticised the plans and argued that automation of sequence did not represent an invention. The scientific advisory committee on the HGP also criticised the plans. Scientists feared that it would fuel a competition for patents and end the collaborative nature of the Project. The issue continued and in August 1992 the US patent office received further applications for patents on 4448 ESTs (Sulston and Ferry 2002) (p. 90). Following the election of President Clinton in November 1992, Healy (a Republican) resigned and her successor Harold Varmus (Nobel Prize winning cancer researcher) withdrew all of the outstanding patent applications in 1994 (Sulston and Ferry 2002).

James Watson resigned in April 1992 amidst a controversial enquiry launched by Healy into his financial position because of a potential conflict of interest. This enquiry was partly prompted by Watson's efforts to secure funding for John Sulston and Bob Waterston to complete their work on the worm genome and thereby remain with the Project after they were approached by private industry (Sulston and Ferry 2002). Members of the scientific community criticised the enquiry as a mechanism to remove Watson (Wilkie 1993).

Access to the human genome sequence remained a sensitive issue. For example, in 1995 the Wellcome Trust sponsored a meeting in Bermuda to broker a commitment from the international sequencing community into making the information gathered publicly available. The meeting produced the following 'Bermuda Principles':

Automatic release of sequenced assemblies ... (preferably daily), Immediate submission of finished annotated sequence, Aim to have all sequence freely available and in the public domain for both research and development, in order to maximise its benefit to society (Sulston and Ferry 2002) (p.146).

International collaboration was however threatened by the formation of the 'G5' composed of the leading five labs (Baylor College of Medicine, Washington

University, DOE's Joint Genome Institute, Whitehead Institute, and the Sanger Centre). Sulston described its existence as 'a slap in the face' to partners who had considered themselves equal in the consortium and taken part in Bermuda meetings (Sulston and Ferry 2002) (p.193).

The most controversial episode in the origins and development of the HGP came in 1996 when a private company, Celera Genomics, was established to sequence the human genome faster than the public effort by using a different method. Celera, led by Craig Venter, was formed when Venter acquired private support to form a commercial company with Mike Hunkapiller of Applied Biosystems (ABI) (the company who made the sequencers used by most of the genome labs) to sequence the entire human genome in three years (Sulston and Ferry 2002). They proposed using a highly controversial method that involved a new sequencing machine (produced by ABI) that could sequence much faster than other models. Celera proposed to further increase the speed of the process by employing the whole-genome shotgun method that Venter had previously used to sequence bacteria. This meant that Celera proposed to shotgun the whole genome at once, rather than map the clones first and then shotgun-sequence them individually (the method used by the public effort). The public effort discarded this approach (known as the whole-genome shotgun method) because the bacterial genome differed greatly from that of the human (Sulston and Ferry 2002). Venter's announcement lent potency to the Sanger Centre's funding application in May 1997 to double their funds and complete a third of the human genome. They argued that their position as a leading group would be threatened if output was not doubled, and that if there was no strong international force then the Project could be taken over by Celera and access to the genome would not be freely available (Sulston and Ferry 2002).

The different approaches employed led the HGP to be viewed in the media as a 'race' between the privately funded Celera genomics and the international public effort. These efforts were further distinguished in terms of their access agreements. The public effort, comprised of 16 groups in the US, UK, France, Germany, Japan and China, made their results publicly available, whereas Celera restricted the availability of their results within commercial limitations (Glasner 2002). Disagreements between the two efforts over methods and access agreements were increasingly voiced in the

media. In June 2000, *Nature* magazine described it as the ‘scientific rivalry to end all scientific rivalries’ (Macilwain 2000) (p.983). This media battle involved several bitter exchanges between Celera and the international public effort. For example, a letter from Francis Collins to Craig Venter that detailed key differences between the groups and criticised Celera for refusing to restart communication was released to the press in February 2000. In response, Celera accused the public effort of trying to end attempts at co-operation, as it was holding out to strike a deal with another private company (Sulston and Ferry 2002). Also, following Bill Clinton’s and Tony Blair’s declaration that the sequence should be freely available to all researchers, CBS Radio News reported that the President and Prime Minister had agreed to stop the patenting of genes, which caused a considerable stock market fall (Sulston and Ferry 2002) (p. 219). President Clinton was keen to end the dispute between Celera and the public effort. Most Republicans supported Celera and sought support from the biotechnology industry that had suffered in the markets whereas most Democrats backed the publicly funded effort. Ari Patrinos of the DOE brokered the peace, and his efforts resulted in an agreement to have a joint announcement of completion of the draft sequence on the 26 June 2000 (that featured the then President Bill Clinton and Prime Minister Tony Blair), a simultaneous publication of the results, and an end to the competition in the media (Sulston and Ferry 2002). Following these negotiations, Collins and Venter agreed to an interview with *Time* magazine entitled ‘The race is over’ (featuring a picture of them in their lab coats standing next to each other, smiling) (Roberts 2001) (p.1190).

Controversy remained however as Celera refused to display their data in the public databases, which had ramifications for publication of the draft sequences. The agreement reached between *Science* (the usual choice for joint publications) and Celera regarding access included a number of terms. Commercial companies and academics would have to sign a material transfer agreement, under which academic users could download 1 megabase per week via Celera’s website (subject to a non-distribution clause). If academic researchers wanted further access a signature from a senior member of their department would be required to guarantee that data would not be redistributed. Commercial companies would have to pay to use the data and were restricted by agreements not to redistribute them (Sulston and Ferry 2002). As a result of these terms, the public effort changed publishers to *Nature* magazine. In publishing

its paper, the international group stressed the collaborative nature of their effort by naming the author as the ‘International Human Genome Sequence Consortium’ rather than individual names. They included twenty centres as members of the consortium: twelve from the US, five from Europe (one from UK, one from France and three from Germany), two from Japan and one from China. Countries that had made smaller contributions were listed in the acknowledgements. Publication of the two papers took place simultaneously in different outlets on the 12 February 2001 (Sulston and Ferry 2002).

### 1.3 International Context of National Genetic Databases

Once the human genome had been sequenced, a number of countries and groups of scientists wanted to use the new knowledge to help them understand the genetic basis of human diseases and response to the environment. The development of this more applied study required large population samples in order to have enough genetic and environmental variation and the statistical power to establish genetic linkages even with common diseases since these tend to be multifactorial and multiple gene based. The completion of the HGP thus heralded proposals for many national genetic databases worldwide. For example, national genetic databases were set up or proposed in Estonia, Latvia, Sweden, Singapore, Tonga, Spain and the United States (Austin, Harding et al. 2003). By far, the most controversial of these projects was set up in Iceland.<sup>15</sup> I will describe the origins of the Icelandic database and assess how the controversy over its consent procedures affected the origins and development of other national genetic databases.

In December 1998, the Icelandic government passed the Health Sector Database Act (HSD Act) that permitted the Ministry of Health and Social Security to contract out the construction of a national genetic database (HSD). In 1999, the government granted deCODE Genetics (who proposed the HSD Act) an exclusive license to produce and manage the database. Under the Act, deCODE incorporated the HSD in its Genealogy Genotype Phenotype Resource (GGPR) programme, which links together three databases: a genetics database, a genealogical database and the HSD (Merz, McGee et al. 2004). DeCODE would be the only company able to use the data commercially for twelve years (Martin and Kaye 2004). DeCODE genetics is a private biotechnology company in Reykjavik, Iceland. It was established in 1996 to do population genomics research into common diseases. They set up research programmes on the genetics of 35 common conditions such as cancer, heart disease, diabetes and Alzheimer's. DeCODE works closely with the Swiss pharmaceutical company Hoffman La Roche who are collaborating on twelve of the above programmes, and pay \$200 million over 5 years to access the results (Martin and Kaye 2004).

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<sup>15</sup>For further discussion of the ethical issues involved in the Icelandic database see: (Coghlan 1998), (McInnis 1999)

DeCODE have unique resources with which to do such a study, including Iceland's comprehensive genealogical records, a well-developed health care system, medical records of the entire country since the First World War, and a large collection of tissue samples stored since World War Two. Due to the genetic homogeneity of the population, the task of detecting disease-related gene variants is significantly less complicated (Martin and Kaye 2004). The lack of immigration to Iceland has led to the virtual genetic isolation of the population (Berger 1999). It is proposed that the Icelandic database will hold medical, genealogical and genotype data, and data on diagnoses, treatment response and costs, length and place of treatment. It aims to discover the genetic causes of disease by using genealogical data to group together individuals with a particular disease into large extended families (<http://www.decode.com> 2003) (accessed 29/10/03). It proposes to use such knowledge to develop drugs and diagnostic tools.

Controversy has accompanied the development of the Icelandic database largely because of its commercial nature, ethical procedures, and identifiable health information from citizens' medical records. For example: 'DeCODE's proposal to build the HSD and use it in its GGPR has been one of the most thoroughly debated and analyzed biotechnology ventures in history' (Merz, McGee et al. 2004) (p. 1). Its opt-out consent procedure is however the single most inflammatory issue (Martin and Kaye 2004). DeCODE are not required to obtain Icelanders' informed consent before their medical records are included in the database: rather, they can opt out by completing a form that records their wish not to participate. By completing this form Icelanders can prevent any new information on them being added to the database (Greely 2001). Following an agreement in August 2001 between deCODE, the Icelandic Medical Association (IMA), and the Director General of Public Health, deCODE permitted citizens to have their data removed from the HSD after collection. This agreement thereby removed one of the most controversial aspects of the HSD Act that allowed citizens to only stop future data collection by opting out. The IMA withdrew its opposition to the GGPR project as part of this agreement (Merz, McGee et al. 2004). This aspect accounted for some of the most serious international criticism; for example the initial draft of the bill was criticised internationally by the European Union's Data Protection Commissioners for not complying with

internationally recognised safeguards protecting the rights of participants (Coghlan 1998).

Observers have also criticised the private nature of its funding and commercial influence on the project. Scientists especially criticised the monopoly held by deCODE and Hoffman-La Roche as those who do not work for those companies would be excluded (Berger 1999). Mannvernd, an organisation on research ethics set up in response to the Health Sector Database Law, were especially critical of the ethical procedures and the opt-out consent policy in particular (Greely 2001).

Proponents of other national genetics databases paid particular attention to ethical, legal and social issues, particularly consent, to avoid the controversy that accompanied the early stages of the Icelandic database. For example, these proponents have stressed the importance of informed consent to their initiatives. They have gone to considerable lengths to develop sound ethical procedures, such as extensive consultation exercises with the public, to disassociate themselves from the Icelandic example. Such was the controversy surrounding the ethical procedures adopted in the Icelandic database that no other resource emulated their approach (Greely 2001). As Jon Merz et al state: 'While it has yet to be followed elsewhere, the Iceland model provides an informative counterexample that must be critically examined by others considering similar ventures' (Merz, McGee et al. 2004) (p. 7).

UK Biobank therefore emerged in the context of two scientific enterprises, the HGP and Icelandic database, that aroused considerable controversy focussing on the role of commercial companies in large scale genetic research. This needs to be taken into account when trying to understand some elements of the proposed organisation of UK Biobank (in particular the strong emphasis on ethics and public consultation, and the stress on an 'equal playing field' in terms of access to the data).



## 1.4 Description of UK Biobank

I will now give a brief overview of UK Biobank in order to contextualise the literature review below. I provide a detailed account of the origins and development of UK Biobank in chapter two. The overview at this point is largely based on information from the UK Biobank website in 2006,<sup>16</sup> and thus mostly represents recent descriptions of UK Biobank. However, it is also based on data from previous versions of the website from 2004-2005<sup>17</sup> and information regarding the organisational changes is partly based on interviewees' accounts.<sup>18</sup>

UK Biobank is an endeavour to construct a national UK genetic database of health and lifestyle data, including blood and urine samples, of half a million volunteers aged between 40 and 69 years old (<http://www.ukbiobank.ac.uk/about/overview.php> 2006) (accessed 19/12/06). Their health will be monitored through their medical records for up to thirty years. The age group was chosen as individuals within this age range are at risk from the types of diseases that UK Biobank would investigate.

*'This age group is being studied because it involves people at risk of developing serious diseases – including cancer, heart disease, stroke, diabetes, dementia – over the next few decades'*  
(<http://www.ukbiobank.ac.uk/about/why.php> 2006) (accessed 19/12/06)

The premise is that, over the next twenty to thirty years, UK Biobank will allow researchers to study the development of diseases such as cancer, heart disease and Alzheimer's to improve methods of prevention, diagnosis and treatment. It is suggested that UK Biobank will be in a better position than previous, smaller-scale attempts to discover why some people develop particular diseases and others do not, and assess the contribution of genes, lifestyle and environment to the development of

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<sup>16</sup> [www.ukbiobank.ac.uk](http://www.ukbiobank.ac.uk)

<sup>17</sup> The UK Biobank website underwent significant alterations in terms of presentation and content during the period of my research.

<sup>18</sup> Detailed information regarding the nature of the organisational changes was not available on the UK Biobank website.

different diseases (<http://www.ukbiobank.ac.uk/about/why.php> 2006) (accessed 19/12/06).

*‘Scientists have known for many years that our risks of developing different diseases are due to the complex combination of different factors: our lifestyle and environment; our personal susceptibility (genes); and the play of chance (luck). Because UK Biobank will involve thousands of people who develop any particular disease, it will be able to show more reliably than ever before why some people develop that disease while others do not. This should help to find new ways to prevent death and disability from many different conditions’*

(<http://www.ukbiobank.ac.uk/about/why.php> 2006) (accessed 19/12/06)

It is proposed that access to the data and the samples will be available in anonymised form only to scientifically and ethically approved researchers, national and international, public and private. UK Biobank is funded by the MRC, the Wellcome Trust, the DoH and the Scottish Executive. The initial funding figure was £45million but it increased in 2004 and the funding committed to date is approximately £62 million (<http://www.ukbiobank.ac.uk> 2005) (accessed 10/04/05).

According to the website in 2006, the half-million sample will be identified from central registries, from which UK Biobank has confidential access to name, address, sex, date of birth and general practice details. Those selected will be sent an invitation letter directly from UK Biobank, and general practitioners will be informed that their patients may be invited to participate in UK Biobank. Participation in UK Biobank will involve attending a local study assessment centre for an hour and a half to answer questions, give blood and urine samples, and have some standard measurements taken. Participants will be required to consent to their health being monitored for many years by UK Biobank directly through routine medical and other records, and to being re-contacted by UK Biobank to answer additional questions and/or attend another assessment visit, which would be optional (<http://www.ukbiobank.ac.uk/about/why.php> 2006) (accessed 19/12/06).

*'People to invite into UK Biobank are identified from central registries. The only information provided, in confidence, to UK Biobank is name, address, sex, date of birth, and general practice. These details are processed centrally (in accordance with the Data Protection Act) and an invitation letter sent directly by UK Biobank. General practitioners are advised that people registered with their practices may be invited to take part'*

(<http://www.ukbiobank.ac.uk/about/why.php> 2006) (accessed 19/12/06)

I provide a detailed chronology of events in the development of UK Biobank in chapter two. In brief, the first official meeting between the MRC and the Wellcome Trust regarding UK Biobank was in 1999. After international peer review of an initial scientific protocol and various consultation exercises with the public and professional groups, the funding bodies made the decision to fund UK Biobank in 2002. Following the funding decision an organisational structure was put in place and the first pilot study began in February 2005. The original CEO of UK Biobank Limited, John Newton, who was appointed in March 2003, resigned in December 2004; Rory Collins was appointed as the new CEO *and* Principal Investigator (PI) in August 2005. After the appointment of Rory Collins, significant changes were made to the organisational structure.

I describe the organisational structure and the changes made to it in chapter two but I will briefly introduce one important aspect now. Before the changes, the organisational structure was based on a 'hub' and 'spoke' model. In this model, the hub was to have overall responsibility for delivering UK Biobank including financial management and storage of the data and samples, and it was to co-ordinate the activities of six spokes. The spokes were to be responsible for recruitment and initial data and sample collection from primary care (<http://www.ukbiobank.ac.uk/organisation.html> 2004) (accessed 23/04/04). Following the organisational changes, initial data and sample collection were to be managed centrally via the hub, and spokes were given the opportunity to compete for contracts to carry out operational tasks. Additionally, the hub was no longer responsible for

overall delivery of the resource, which was given to a newly created Implementation Group (<http://www.ukbiobank.ac.uk/news/pr/8aug05.php> 2005) (accessed 10/11/05).

## 1.5 Literature Review

### *Introduction*

As my study is an example of the history of contemporary science, and UK Biobank can be regarded as a ‘Big Science’ project (this issue is explored in the conclusion), my literature review concerns the development of the history of contemporary science as an academic field, the concept of Big Science, and the origins and development of Big Science projects. The history of contemporary science is a contested discipline. As such I felt that it was important to seek understandings of the field in the literature to aid analysis of the issues involved in my study of UK Biobank. The relationship between UK Biobank and the HGP, and the latter’s association with the beginning of Big Science for biology renders a review of Big Science projects and the term itself useful. Hence, analysis of the origins and development of Big Science projects should enable a better understanding of the history of UK Biobank.

To explore the history of the HGP and of Big Science more broadly, I selected articles using the search engine JSTOR and the following journal groupings: sociology, philosophy, history and history of science and technology. I used the following keywords: ‘Histor\* of contemporary science’, ‘Big Science’, ‘Human Genome Project’. Although these searches were broad, my focus on the historiography of contemporary science, Big Science and Big Science projects allowed me to narrow the results. I searched the bibliographies of particularly useful articles to identify further relevant literature. The advice of colleagues and contacts in relevant disciplines also furnished me with additional literature.

Given the evolving nature of UK Biobank and its international counterparts, there is not a body of literature that concerns the origins and development of national genetic databases. What literature is available on national genetic databases tends to concentrate on the ethical<sup>19</sup> issues involved or the scientific<sup>20</sup> merits of the research.

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<sup>19</sup>For discussion of ethical issues see: (Johnston and Kaye 2004), (Greely 2001), (Martin 2001), (Anderlik and Rothstein 2001), (Kaye and Martin 2000), (McHale 2004), (Tutton, Kaye et al. 2004), (Macintyre 1997), (Lowrance 2001), (Tutton and Corrigan 2004), (Corrigan 2004), (Hoeyer 2004), (Kaye 2004), (Weldon 2004), (Lewis 2004), (Tancredi 1994), (Glasner and Rothman 2004), (Gottweis 2005), (Willis 2005), (Williams and Schroeder 2004), (Berg 2004), (Corrigan 2003)

<sup>20</sup> For discussion of scientific issues see: (Black and Payne 2002), (Black 1999), (Watson, Shickle et al. 1999), (Bayat 2002), (Kinmonth, Reinhard et al. 1998), (Collins, Green et al. 2003), (Collins and

There is however a substantial amount of literature on the Sociology of Scientific Knowledge (SSK)<sup>21</sup>, which emerged in the 1970s and focussed on the technical and cognitive as well as the social organisation of science. Proponents stressed the social nature of science and thereby studied its content rather than its context (Nicolson 1993). *The Cancer Mission* by Kenneth Studer and Daryl Chubin is cited as an important example of this field: '[it] drew attention to the way in which the social organisation of science in its turn impacted on the organisation and hence the content of biomedical science' (Berridge 2005) (p. 17). This approach was not however relevant to my research as UK Biobank had not begun recruitment when I started my research, and hence there was no scientific activity that I could have studied.

I have divided the literature review into two parts; the first explores the historiography of contemporary science, and the second investigates the concept of Big Science and the origins and development of Big Science projects.

### 1.5.1 Historiography of Contemporary Science

#### *1.5.1 (a) The history of contemporary science*

##### *Imbalance toward pre-twentieth century science*

The history of science is weighted toward periods prior to the twentieth century. Traditionally, historians of science avoided recent science and believed that scientists were the most appropriate people to undertake such research. As Thomas Soderqvist stated:

Only one or two decades ago most historians of science considered recent science – the scientific culture created, lived and remembered by contemporary scientists – an area of study best left to the historical actors themselves (Soderqvist 1997) (p. 1).

Despite the fact that most scientific activity has taken place in recent times, the majority of historians of science concentrate on scientific activity pre-1945, which Soderqvist described as a 'paradoxical temporal imbalance' (Soderqvist 1997) (p. 3).

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McKusick 2001), (Bumol and Watanabe 2001), (Clayton and McKeigue 2001), (Barbour 2003), (Bell 1998)

<sup>21</sup>See the following for examples of SSK: (Studer and Chubin 1980), (Latour and Woolgar 1979)

Historians of science have identified a number of explanations for this imbalance. One explanation is insecurity regarding the professional status of the history of science as an emerging discipline. It has been suggested that historians of science studied pre-twentieth century science to avoid accusations of partisanship and presentism and feared 'inviting the bias which is said to accompany a lack of historical distance' (Soderqvist 1997) (p. 1). However, historians of contemporary science have increasingly challenged this argument that objectivity is not attainable in researching recent events. For example, Margaret Gowing, the historian of British Atomic Energy, stated that 'the argument that truth is proportional to distance in historical perspective has seemed increasingly fallacious' (Gowing 1964) (p. xiii).

A second explanation is the relationship between the history of contemporary science and science, specifically the latter's attachment to the natural sciences rather than the arts or social science. For example, history of science was traditionally part of the undergraduate natural sciences syllabus rather than of the social sciences or history syllabi (Gowing 1975) (p. 9). Such a close relationship between the history of contemporary science and the natural sciences accounted for a lack of focus on its social and political context. Gowing criticised this aspect of the development of the history of science:

It has been predominantly, though by no means exclusively, an internalist subject concerned with pure science, and as some historians have looked increasingly at science in relation to society, they have been called externalists (Gowing 1975) (p. 24).

Methodological issues are a third explanation for the lack of historical study of recent science, specifically the question of scientific training and the relationship between historian and scientist in undertaking research. Some historians of science argue that historians should undertake scientific training in the discipline researched and attribute the lack of historical research on contemporary science to its increasing complexity. For example, Soderqvist stated: 'One of the main reasons why historians have hesitated to deal with recent and contemporary science is probably that such familiarity is very difficult to obtain without systematic and professional scientific training' (Soderqvist 1997) (p. 9). Others argue that scientific training is not necessary

to research contemporary science and point to the requirement of all historians to understand various complicated concepts and theories, such as aspects of theology or economics (Gowing 1975). Gowing has criticised suggestions that contemporary historians require a science degree to undertake research on contemporary science: '[s]uch suggestions are dangerous and should not be offered as alibis to reluctant historians, for science can be studied in many areas, from many aspects and from different levels' (Gowing 1975) (p. 10).

A further explanation for the lack of history of contemporary science is the difficulty of establishing an appropriate relationship between historian and scientist, particularly in conducting oral history interviews. Soderqvist argued that scientists' respect for historians of earlier historical periods does not extend to historians of contemporary science:

When it comes to recent and contemporary science, however, scientists often find it difficult to acknowledge the need for specific historical skills. Scientists sometimes find it hard to realize that the problems addressed by historians are of a different kind than those asked by the scientist (Soderqvist 1997) (p. 10).

These comments reflect historians' and scientists' different understandings of the nature of historical research, which is discussed in the next sub-section. Critics of the history of contemporary science largely refer to the influence of the historian on the research: 'History can only be written about periods in which the historian does not have a stake in what happens because the issues of greatest concern to the historical agents no longer have the same relevance' (Fuller 1997) (p. 245). These critics therefore conceived of the role of the historian of contemporary science narrowly in terms of preserving data for future historians.

Historians of contemporary science have criticised the imbalance between history of recent events and earlier periods. They have stressed the significance of recent events and argued that they should be researched just as much as earlier periods: 'it has seemed increasingly absurd that the events of the last thirty years which have so powerfully shaped our lives should be the least recorded by historians and the most obscure to the younger generation' (Gowing 1964) (p. xiii). Historians of contemporary science argue that recent science should be studied because of the significant growth of scientific activity in the latter part of the twentieth century. For



example, more than 90% of all scientists who ever existed in world history have been active since the end of the Second World War (Soderqvist 1997) (p. 2). Historians of contemporary science stress the contemporary nature of all history and the relevance of the present in analysis of the past (Lindee 1997). This position is particularly prevalent in the United States where historians continue to ‘expect history to shed light on contemporary concerns’ (Lindee 1997) (p. 40).

The history of contemporary science has however begun to receive more attention. For example the percentage of publications listed in *ISIS Critical Bibliography* concerning the twentieth century (i.e., since 1914) as a percentage of all chronologically arranged publications rose from about 10% in the early 1970s to about 30% in the late 1980s (Soderqvist 1997) (p. 3). Historians of contemporary science attribute this increase to the growing security of the field. The increasing focus on recent science in the history of science has been accompanied by an even greater shift towards recent science in the field of science studies, such as the sociology of science, sociology of scientific knowledge (SSK) and science policy studies (Soderqvist 1997).<sup>22</sup>

#### *1.5.1 (b) Relationship between historian and scientist*

##### *Contested Territory*

The relationship between historian and scientist is complicated in the history of contemporary science as the field represents a contested territory between active scientists and historians, as well as competition from a range of professional disciplines including science journalists and sociologists of science (Soderqvist 1997). Competition between historians of contemporary science and active scientists is problematic on account of different articulations of the nature of the history of science, which have characterised its development as a professional discipline. For example, Soderqvist describes ‘professional conflicts and mutual accusations of ‘naïve realism’ and ‘higher superstition’’ (Soderqvist 1997) (p. 11).

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<sup>22</sup>For example: (Jasanoff 2000)

The development of the history of science was shaped by different articulations of the field as either scientific or historical. Scientists, rather than historians, were the main proponents of the discipline, and the researcher often assumed the identity of scientist-historian. Scientists' understandings of the nature of the history of science were therefore dominant. As the discipline developed, attitudes towards the history of science changed, and historians' articulations of the field became influential. This shift was accompanied by greater interest in the influence of social and political factors in the constitution of knowledge, reflecting adoption of a more relativist approach (Hughes 1997). The shift resulted in professional conflicts between those historians who adhered to the new attitudes, and those scientists who did not. Some scientists felt that the new approach adopted by historians of science threatened the legitimacy of science itself, and its theoretical grounding in positivism. For example, Jeff Hughes stated:

In recent years, a relatively small number of scientists, suspicious of historians' non-whiggish and non-celebratory histories and of their increasing independence from science, see historians and those with whom they intellectually associate as somehow attacking the "moral stature", "epistemological authority", and therefore the legitimacy of science (Hughes 1997) (p. 22).

Scientists attribute such an 'attack' on science to many historians' departure from empirical understandings of a universal 'truth'. For example, Joseph Tatarewicz commented: 'Historians...have largely abandoned the hope for a single, definitive, true account. Actors, however, can be decidedly uncomfortable with the notion of multiple and superseded histories' (Tatarewicz 1997) (p. 77). Given historians' dependence on scientists for source material, these tensions between them represent a distinguishing feature of discipline.

The question of whether the history of science should serve to legitimise scientific activity represents a key difference between scientists' and historians' articulations of the field. For example, Hughes describes a

conflict emerging between those who seek to preserve the history of science as a grand narrative of progress and utility and those who seek to write a more *critical*, differently *engaged* and, so it could be argued, more *relevant* kind of history of science (Hughes 1997) (his emphasis) (p. 31).

Scientists tend to believe that history should serve such a legitimising function in an existing or emerging field whereas historians tend to disagree. Hughes does not believe that history should serve to legitimise science:

While attention to the technical content of science is, and must remain a centrally important part of the history of science, however, this notion of history as somehow adjudicating over past science should not go unchallenged, for it seems to me to raise important questions about the role of the historian and of historical writing about the sciences (Hughes 1997) (p. 25).

Historians of science question the validity of scientists' motives in producing accounts that seek to legitimise scientific activity: 'For reasons we (and, one suspects, they) understand perfectly well, for example, scientists tend to write largely celebratory, teleological and/or anecdotal accounts of the past' (Hughes 1997) (p. 26).<sup>23</sup>

Some scientists go as far as claiming that historical accounts that do not evaluate science should not be described as history of science:

For some scientists, moreover, history is so valuable a resource that to write history which doesn't legitimate science in some way is actually seen as positively *delegitimizing* – in other words, as 'undermining' science in some sense – which can generate a profound hostility towards professional historians of science and their writings (Hughes 1997) (p. 28).

The scientist Lewis Wolpert has criticised sociologists, philosophers and historians of science for not adhering to the values of scientific rationality, and for studying the processes by which knowledge is created and constituted rather than 'what institutional structures most favour scientific advance, what determines choice of science as a career, how science should best be funded, how interdisciplinary research can be encouraged' (Wolpert 1992) (p. 122). Although these sentiments are not indicative of the majority of scientists, the debate is highly relevant. For example, scientists at a conference on 'The Social Standing of Science' at Durham University in 1994 rejected the sociology of scientific knowledge and sociologically-informed

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<sup>23</sup>For a wider discussion of these issues see: (Forman 1991)

history of science for not contributing to science or understanding of science as a social phenomenon (Hughes 1997) (p. 29).

Scientists' expectations of the history of science as legitimising scientific activity are particularly problematic in contemporary science when scientific studies do not develop as intended. For example, Ilana Löwy was granted access to the clinical trial of interleukin-2 (IL-2) because the scientists wanted a reliable witness to a successful trial, but her presence was less welcome when the trial did not develop as expected.

As Löwy found:

The presence of 'our historian' was seen as an asset in the early stages of the IL-2 trial when a straightforward triumph was expected, but became problematic when this clinical experiment turned out to be a much more complicated enterprise (Löwy 1997) (p. 98).

#### *The 'official' historian*

The relationship between scientists and historians of contemporary science is particularly complicated in the case of commissioned histories, which are more common in the history of science. The historian's autonomy is under scrutiny when they are funded by the same scientists they are researching. Commissioned research therefore presents the historian with specific challenges. Given their proximity to the events they are researching, historians of contemporary science can find it particularly difficult to distance themselves from their patrons. As David Cantor stated: 'Critical distance is difficult enough to achieve when writing twentieth-century history, a distance shortened by the purse-strings and obligations of contract work' (Cantor 1992) (p. 132). Historians must carefully negotiate their role with the patrons or they may find themselves 'constrained by the real and imagined needs and wishes of their patron, often pull their punches and produce pseudo-celebratory histories which toe the patron's line' (Hughes 1997) (p. 30). Gowing acknowledged these challenges but reported that she did not experience them and did not distinguish them from those facing the non-official historian (Gowing 1964). Scientists can exert considerable influence in defining the scope of the history of contemporary science by funding official historians. The type of studies they choose to support reflects their perception of the legitimising role of the history of science. For example, Tatarewicz commented: 'with rare exceptions the historical work will be focussed only on

‘successful’ or ‘significant’ projects, those so defined by the actors themselves and for which they are willing to provide the money’ (Tatarewicz 1997) (p. 72). In commissioning historical studies scientists encounter advantages and disadvantages. On the one hand, they avoid accusations of bias by appointing a historian rather than a scientist. On the other hand, the appointed historian may not share their perception of the legitimising role of the history of science. In short, ‘they [scientists] relinquish some of their control over history but may be repaid by gaining credibility’ (de Chadarevian 1997) (p. 63). The role of the official historian can be the only role available to the historian of science, not just because of scarce financial support but because of the nature of the research. For example, it would be very difficult to get access to official documents that are not available to the public if the research is particularly sensitive, unless the historian undertook an official role. Gowing reported that the documents she accessed in researching British Atomic Energy were such that a non-official role would have been inappropriate:

It would be extremely difficult to give to someone without any official standing the freedom to roam among these records, some of which still contain very sensitive material ... The official historian’s official standing, his ties with a Government organisation, his signature of a declaration under the Official Secrets Act, make it possible for Government servants to speak freely to him and give him access to their papers (Gowing 1964) (p. xiii).

### *Methodological Issues*

Methodological issues regarding the relationship between historian and scientist are an important feature of the history of contemporary science, which set it apart from the history of earlier scientific activity. These issues primarily concern scientists’ expectations of their role as interviewees, and issues of confidentiality. The historian of contemporary science must carefully manage social relationships with the scientists on whom they rely for source material. Scientists’ understandings of their role as an interviewee can differ from that of historians, which complicates research when divergent understandings collide. For example, Soderqvist stated:

Scientists are often unwilling to take the time and effort to try to understand the aims of historians, and often tend to believe that their main contribution to the co-operative effort is to ‘set the historical record right’ instead of seeing

themselves in the role of witnesses and scientific experts (Soderqvist 1997) (p. 10).

Historians of contemporary science also bear significant social responsibilities to the scientist, which further complicates the relationship between scientist and historian. The historian must consider what information to include and what to omit from published findings and assess the ramifications for the scientist, professionally or personally, of these decisions. For example, the historian must assess whether or not particular information could influence the renewal of grants (Lindee 1997). These issues are particularly significant in the history of contemporary science given the historians' reliance on scientists for source material. It is argued that the issue of confidentiality is particularly complicated in the history of contemporary science as the tools employed by other researchers, mainly the use of anonymity, are not appropriate for the historian. For example, Susan Lindee stated:

Historians by disciplinary agreement do not (cannot) employ the methodological buffering mechanisms of the journalist, anthropologist, or sociologist. A historical account is specific rather than universalizing; actors in a historical account are so important they must be named; and the historical account depends on long-term, intimate knowledge<sup>24</sup> (Lindee 1997) (p. 42).

### 1.5.2 'Big Science'

#### *Introduction*

I will now review the literature concerning the term Big Science and the origins and development of Big Science projects. As discussed in the introduction of 1.5, such a review is both relevant and useful given perceptions of UK Biobank as a Big Science project, and the association of the HGP with the beginning of Big Science for biology (given the relationship between UK Biobank and the HGP). The Manhattan Project, set up during the Second World War to design and produce atomic bombs, is often regarded as the beginning of Big Science and representing a turning point in twentieth century science from pre-war 'little science' to post-war Big Science. It involved

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<sup>24</sup> My contemporary history of the origins and development of UK Biobank differs from traditional accounts of contemporary history of science in that I maintained the anonymity of my sources, which will be discussed in the methods chapter.

American and British scientists from a variety of professional backgrounds including engineers and technicians, 130,000 people were employed at its height and its total cost was \$2 billion (Hughes 2002) (p. 9). The Project involved powerful alliances between military, academic and industrial scientists and a strongly hierarchical and complex organisational structure. Historians of science have however debated the extent to which the Manhattan Project caused the transition from little science to big science (this is discussed in 1.5.2 (d)). To place my analysis of Big Science in context, I begin by describing three examples of Big Science projects, the MRC AIDS Directed Programme, the Centre Européen de Recherche Nucléaire (CERN), and the Space Telescope. I selected these projects, as well as the HGP (described earlier), as their origins and development resonate with those of UK Biobank in that they experienced organisational difficulties and involved establishing a resource, be it the human genome sequence, funding research into finding an AIDS vaccine, a Space Telescope or a high-energy physics laboratory (in the case of CERN). Second, I will explore the origins and contemporary understandings of the term Big Science. Third, I examine four key characteristics of Big Science Projects: scale, social and political context, sponsorship and organisational issues largely in relation to these projects. Last, I will address criticisms of Big Science.

#### *1.5.2 (a) MRC AIDS Directed Programme*

Following the production of a document that called for a large MRC programme in AIDS by a ‘ginger group’ of Royal Society fellows, the then Secretary of the MRC, Sir James Gowans (with the support of the then Chairman, Earl Jellicoe) produced plans for an MRC AIDS Directed Programme to fund research into finding an AIDS vaccine and develop viral chemotherapy. Gowans presented these plans with David Tyrrell (Chairman of the AIDS Working Party) and Ian Weller (from the Middlesex Hospital, London) to the Cabinet Committee on AIDS in December 1986. The document suggested that Britain might lead the world in the search for a vaccine and that results would be available within five years (Berridge 1996). The Cabinet committee granted Gowans (who became the first director of the programme) an initial £1m, and in February 1987 further proposals for a £14.5 million research programme were successful. The majority of the funds were allocated to an MRC Directed Programme on AIDS that would focus on the basic science required to

discover an AIDS vaccine. By 1991, the MRC AIDS Directed Programme was costing £9-10m per year (7-10% of the MRC's total budget) (Berridge 1996) (p. 118). In 1993 the then Secretary of the MRC, Dai Rees appointed and chaired a review committee into the Programme. The review was partly prompted by the DoH's decision to gradually remove ring-fenced funding on AIDS to the MRC and the issue of whether AIDS should have separate budget within the MRC (Berridge 1996).

The Programme had a significant public profile and represented an elaborate organisational structure with a central secretariat and scientific working groups on different topics:

It was based on a model of closely linked, directed research, with regular working group meetings between scientists, monitoring of progress, special arrangements for collaboration with industry and specialised centralised facilities (Berridge 1994) (p. 136).

As Virginia Berridge reported, a scientist involved in the MRC AIDS Directed Programme described it in the following terms: 'The level of integration is unique. It's a mini-Manhattan' (Berridge 1996) (p. 177). The Programme had a considerable training element, for example there were twenty PhD awards in virology and immunology and post-doctoral funding for study abroad. Category-3 laboratories (for growing the virus) were established at Cambridge, Glasgow, the Chester Beatty in London, and the National Institute for Biological Standards and Control (NIBSC). Critics of the Programme referred to its focus on basic science and lack of activity in clinical science. Gay activists argued that the focus on basic science in developing a vaccine had more political clout than a clinical focus on treatment of those already infected (Berridge 1996).

Industrial links were an important part of the AIDS Directed Programme, which brought scientists and industry to far greater levels of collaboration and strengthened existing relationships. Efforts to develop a vaccine prompted the MRC, via the Programme, to sign co-operative agreements with industrial companies, such as Celltech and British Biotechnology (Berridge 1996). General collaborative research agreements were also signed with various companies. Both types of agreement contained stipulations that industrial companies would contribute to the research



project. Contracts detailed procedures regarding intellectual property, commercial exploitation rights and publication of results (Berridge 1994).

The MRC's AIDS Directed Programme represented a considerable shift in MRC policy from responsive research funding (evident in the MRC AIDS working party set up in 1983) to proactive research funding. Prior to the establishment of the AIDS Directed Programme, the MRC AIDS epidemiology committee set up in October 1985 represented the only departure from this responsive mode in the early role of the MRC (Berridge 1996). The departure from the responsive mode represented by the AIDS Directed Programme was however temporary and only the HGP reflected proactive research funding (Berridge 1994).

#### *1.5.2 (b) Centre Européen de Recherche Nucléaire (CERN)*

In 1949, the notion of multinational cooperation in nuclear science across Europe began to be considered by several figures involved in nuclear science, including Raoul Dautry, Administrator-General of the French Commissariat à l'Energie Atomique (CEA) and Isidor I. Rabi (part of the American delegation to UNESCO). In December 1949, Dautry had a resolution passed at a European Cultural Conference in Switzerland that recommended a series of studies for the establishment of a European institute for nuclear science. Rabi (partly prompted by the establishment of the Brookhaven National Laboratory in the United States) put forward a resolution to the annual conference of UNESCO in Florence in 1950 that encouraged states to set up one or more regional European laboratories (including one in nuclear science), which was adopted by UNESCO's General Assembly on 7 June 1950 (Pestre and Krige 1992). Specialists in classical nuclear physics and cosmic rays and a group of three important administrators of science, including Dautry, took up these proposals in 1950. In December 1950, Pierre Auger, a specialist in cosmic rays and director of UNESCO's Department of Exact and Natural Sciences, organised a meeting of scientists and administrators in Geneva in which Dautry proposed the construction of the biggest accelerator in the world (Pestre and Krige 1992). Throughout 1951, Auger and scientific consultants refined the proposal and forwarded their recommendations to a European intergovernmental conference in December 1951. The conference recommended the establishment of a temporary organisation that it

granted \$200,000 to develop the technical, organisational and financial details involved and present them to potential member-states within eighteen months. On February 15 1952, all of the nations represented, except the UK, signed an agreement reflecting these arrangements, which came into force in May 1952 (Pestre and Krige 1992).

On May 5 1952, the provisional CERN Council first met and established the technical groups to design the accelerators and plan the laboratory. Geneva was selected as the site for the laboratory and construction of a 25- to 30-billion-electron-volt proton synchrotron was selected. In January 1953, discussion of the convention that would set up the permanent organisation began, and the British government was represented officially on the Council for the first time. Eight of the eleven member-states of the provisional CERN Council and the United Kingdom signed the convention on July 1, 1953, which came into force officially in October 1954. The permanent CERN Council met for the first time on October 7 1954 (Pestre and Krige 1992).

The origins of CERN are to some degree contested. On the one hand, senior figures involved in the origins of CERN have presented its genesis as ‘inevitable’ because of the political environment of the time and the considerable resources involved in the project. For example, they refer to the political popularity of collaborative European bodies, such as the European Economic Community and the impossibility of a single European country having the resources required to establish such a resource. On the other hand, the historians Dominique Pestre and John Krige, argue that ‘no historical “necessity” imbued the birth of CERN, that this laboratory “might not have been” or might have emerged with a very different shape from the one it has’ (Pestre and Krige 1992) (p. 81). Hence, in writing the history of CERN they focussed on the process by which it evolved as well as socio-political factors. Pestre and Krige argue that accounts presenting the birth of CERN as ‘inevitable’ are inaccurate as they present the nature of CERN in 1954 as the original aim:

as if the outcome were the simple, logical, and necessary response to an immutable and unambiguously posed question: how to equip *Europe* with a *prestigious* collaborative institute in *fundamental* nuclear physics (Pestre and Krige 1992) (p. 82) (their emphasis).

They further criticise these accounts by arguing that the European spirit was not as powerful as they portray, as some states were anxious about becoming involved in an initiative that they would not control (Pestre and Krige 1992).

As post-war European countries tended to lack clearly defined science policies or government institutions responsible for scientific research, scientists involved in CERN could act independently of national governments. Indeed, scientists and science administrators were not heavily influenced by the scientific establishment and member states (who funded CERN) and enjoyed considerable independence from them (Pestre and Krige 1992). This autonomy is most clearly illustrated in the CERN Council, its central group composed of scientists and political figures, which was an important part of its origins and development. The Council operated independently from member states even though their representatives sat on it. They controlled the project and were responsible for appointing the CERN Director-General who held a powerful position of leadership. A group of men heavily involved in CERN's origins were at the centre of the Council and exchanged dominant posts between them. Known as the 'founding fathers', they were 'Welded together through a struggle that had lasted for years, determined to see their child prodigy succeed completely' (Pestre and Krige 1992) (p. 85). By maintaining a position of unity, this group prevented direct government intervention. The Council fostered a very close relationship with the European high-energy physics establishment (Pestre and Krige 1992).

The Council's response to a member state's challenge to their authority illustrates their control of the project. In 1961 the British tried to unite other governments who objected to budget increases and decide the upper limit for the CERN budgets for the following three years (Hermann, Krige et al. 1990). In response, the Chairman of the Council at a meeting on December 19 1961 (half of which was devoted to the subject) presented the issue as a political one (rather than financial or scientific) that threatened collaboration. Members pointed to the Convention and stressed the sovereign nature of the Council. Armin Hermann et al described this episode as evidence of

'the jealously guarded autonomy of the Council and the functioning of the pro-CERN lobby at its heart, it shows that the Council regarded itself as the only possible decision-making nucleus, the nucleus which history itself had

established and on which it had bestowed legitimacy, and it makes it clear that the Council members were apparently sufficiently powerful when dealing with their domestic authorities to neutralize any initiative aimed at bypassing them' (Hermann, Krige et al. 1990) (p. 364)

The Council was united by clear goals and competition with the United States lent the project greater significance:

'its cohesion lying in the novelty and importance of what was at stake - to be part of a collaborative scheme in *nuclear* science encompassing no less than a *dozen* states which aimed to beat the American monolith by building the biggest accelerator in the world' (Hermann, Krige et al. 1990) (p. 362) (their emphasis).

The establishment of CERN has been widely attributed to the leading role taken by scientists in the project, especially the CERN Council. Given the considerable role played by politicians, diplomats and state officials in setting up CERN, Hermann et al point to the difficulties of this argument. They argue that the Big Science nature of the project demands the considerable support from these groups: 'this was a *big science* project. And where there is 'big science' there is inclusion in a budget, and so the involvement of politicians, or at least of administrators from the higher echelons of politics' (Hermann, Krige et al. 1989) ( p. 199). However, because of the lack of governmental involvement in the conception of CERN, its goals and governance Hermann et al acknowledge the importance of scientists in driving the project:

'The *initiators* of the project were thus not to be found in the world of politics and diplomacy, nor were the initial *roots* and *motivations*, in spite of the existence of an active European ideal. It is in the scientific *need* felt by scientists and scientific administrators, the need to equip Europe with machines beyond the means of individual countries, that the foundation of the CERN project is to be found' (Hermann, Krige et al. 1989) (p. 200) (their emphasis).

### 1.5.2 (c) *The Space Telescope*

The Space Telescope is a large space observatory with a 2.4 metre primary mirror at its centre. It was originally known as the Large Space Telescope from 1965-1975,

renamed the Space Telescope in 1975, and renamed again in 1983 as the Hubble Space Telescope. NASA, with the support of the European Space Agency (ESA) as a minor partner, managed the Space Telescope's design and development. Following a three-year process, White House and Congress approved the project in 1977. Construction of the telescope began in 1977 and it was launched in 1990 (Smith 1992). Designed to be the most 'powerful optical telescope ever constructed', the project involved considerable resources that rendered the involvement of industrial contractors crucial (Smith 1992) ( p. 187). The design and construction of the Space Telescope thus represented a collaboration of government, industry and academe (Smith 1992).

The process of gaining funding from the federal government was a considerable part of the history of the Space Telescope that reflects significant issues, such as gaining astronomers' support for the project. In the mid 1960s NASA sought to extend the pursuit of space astronomy to a wider group of astronomers (especially ground-based astronomers who were generally critical of the project) to justify the costs and thereby gain political support. As Robert Smith stated: 'securing more potential users would win wider support for optical space astronomy' (Smith 1992) (p. 193). Attracting ground-based astronomers to space astronomy was complicated as each represented different styles of science: ground-based astronomy meant 'little science' whereas space astronomy meant 'Big Science' entailing large teamwork and collaboration with engineers and technicians and working under NASA who led and directed the project (Smith 1992). The relationship between NASA and the astronomers was marked by tension over control of the project (Smith 1989). Given that the telescope was constructed to allow astronomers to conduct research and did not perform any research in itself, control of its scientific operations and the relationship between the telescope and its users were particularly significant issues. Concerns over control prompted astronomers to advocate for the establishment of the Space Telescope Science Institution (Smith 1989).

Ground-based astronomers' criticisms of the Space Telescope, namely that it was connected to the much maligned US Space Program and would be funded at the expense of ground-based astronomy, made the task of gaining their support all the more difficult. Despite their criticism, some ground-based astronomers argued that it

was better to be involved and try to change it from the inside than criticise it from the sidelines. Smith quoted one such astronomer who came to that conclusion:

“You had to accept that if there was going to be space science, and if it was going to be supported no matter what you did, then you had to ride that wild horse, instead of letting people with only half-baked ideas claim the leadership” (Smith 1992) (p. 195).

A committee of astronomers formed in the late 1960s to report on the scientific uses of the Large Space Telescope to the National Academy of Sciences aimed to foster support for the project. The chairman of this group, Lyman Spitzer, a leading astronomer from Princeton, key advocate and public champion of the Telescope, played a crucial role in this task (Smith 1992). In justifying the project and garnering support for it, this group did not examine potential scientific questions that it could address: ‘At this stage, the Space Telescope was essentially “all things to all people” as its advocates sought to bundle as many interests as possible into the proposed instrument’ (Smith 1992) (p. 196). Given the reluctance of some astronomers to become involved in politics and the lack of a lobbying group for the Space Telescope, Lyman Spitzer’s role was especially significant following the House of Representatives appropriations subcommittee’s decision in June 1974 to remove all planning funds for the telescope from the NASA’s budget for the fiscal year 1975 (Smith 1992). Spitzer was very well respected among ground-based and space astronomers and his political experience in lobbying Congress was valuable. Such was his role that the telescope became known by many as the ‘Lyman Spitzer Telescope’ (Smith 1992) (p. 200).

Following the completion of a revised National Academy’s Space Science Board report that supported the Space Telescope as a high priority and the activities of leading advocates, Congress reinstated the telescope to the budget in August 1974 albeit with half the planning funds and a number of other concessions, including the involvement of other countries (Smith 1992). The reduction in funds meant a smaller primary mirror (reduced from 3 metres to 2.4 metres) and a number of other changes (Smith 1992) (p. 202). One particularly telling concession was the name change from the ‘Large Space Telescope’ to the ‘Space Telescope’ as ‘large’ suggested a certain grandiosity (Smith 1992) (p. 191). The telescope was therefore redesigned for a range of reasons that extended beyond the scientific and technical:

The redesigned telescope must therefore be interpreted not as a product of technical and scientific considerations alone but as the result of complicated interaction and interpenetration of technical, scientific, political, economic, institutional, and social forces (Smith 1989) (p. 143).

Congressional difficulties united astronomers and increased their awareness of the importance of political activities, which alongside the role of product champions, particularly Lyman Spitzer, was instrumental in obtaining funding:

Without such entrepreneurship, the telescope could not have been made salable; moreover, for the kind of costly big science that the telescope represented, its advocates came to accept that the mobilization of an entire scientific community was necessary to make it politically feasible (Seidel 1992) (p. 202).

In making congressional concessions the telescope became politically acceptable but at considerable cost to its design, which impacted upon its subsequent development: ‘the course of the telescope’s design and development has to be interpreted to a large degree in terms of a program trapped by its own history’ (Smith 1989) (p. 186).

#### *1.5.2 (d) The term ‘Big Science’*

The origins of the term Big Science are unclear but it was in circulation in the late 1950s and increasingly used in the 1960s (Caphew and Radar 1992) (p. 4). Big Science is difficult to define and has qualitative and quantitative connotations, which are reflected in early proponents’ use of the term. Derek J de Solla Price argued that each generation defined Big Science in comparison to previous scientific activity (Price 1963), whereas Alvin Weinberg defined Big Science in quantitative terms as a scientific project that consumed a noticeable portion of the gross national product (Weinberg 1967).

Weinberg, credited with coining the term, was critical of the phenomenon, specifically its effect on the professional status of scientists and non-governmental sponsorship. He argued that competition for funds compromised scientists’ professional integrity and cast them in a role akin to journalism (Weinberg 1967). A science policymaker, he feared that the development of Big Science would be to the detriment of science in general on account of its costs, reliance on public finance, and

the increasing role of scientist-administrators (Capsheew and Radar 1992). Yet he stressed the inevitability of Big Science as a stage in the development of science and defended its place:

Big Science, with all its dangers, does have a real place in the scheme of things. When the end to be achieved is important enough, and when the state of the science suggests that more support will lead to more results...then we are justified in going all out in our plea for public support (Weinberg 1967) (p. 114).

He argued that resources for Big Science should be distributed according to the project's 'social merit or relevance to human affairs and the values of man' (Weinberg 1967) (p. 76). Price, a physicist turned historian, increased usage of the term Big Science with the publication of *Little Science, Big Science* in 1963. He focused on the issue of scientific growth and interpreted Big Science as 'an uncomfortable brief interlude between the traditional centuries of Little Science and the impending period following transition' (Price 1963) (p. 32). Although he argued that the transition occurred in the 1940s or 1950s, he did not believe that the Second World War was a major factor in it. In focusing on the issue of scientific growth, Price rejected firm distinctions between little science and Big Science, and pointed to historical examples of Big Science such as the huge electrical machines in Holland in the eighteenth century (Price 1963) (p. 4). He argued that the transition from Little Science to Big Science was less dramatic and more gradual than appears at first:

For one thing, it is clear that Little Science contained many elements of the grandiose. And, tucked away in some academic corners, modern Big Science probably contains shoestring operations by unknown pioneers who are starting lines of research that will be of decisive interest by 1975 (Price 1963) (p. 3).

Contemporary proponents stress the limitations of fixed and singular definitions of Big Science, such as a quantitative definition in terms of technological capacity. For example, Bruce Hevly argued that: 'Big Science is not simply science carried out with big or expensive instruments...such instruments, despite their size, may be used in a manner consistent with traditional, little science' (Hevly 1992) (p. 356). Similarly, Peter Galison pointed to the influence of different cultures on Big Science (such as academic, military and corporate) as evidence of the many different types of Big Science, and criticised the tendency to apply a singular definition: 'Perhaps because



of its sheer size, historians, sociologists, and scientists have all tended to think of large-scale research as being all of a single type' (Galison 1992) (p. 2). James Capshew and Karen Radar reflected on how the same aspects of Big Science could be interpreted differently, for example it is perceived as an instrument in literal and metaphorical terms:

some studies have emphasized the instrumental dimensions of Big Science, either in the literal sense of its technological components or in the metaphorical sense of its use to serve conjoined political and cognitive goals (Capshew and Radar 1992) (p. 8).

Contemporary proponents of the term also stress the significance of the growth of scientific activity and the relativity of the term 'big'. For example, Capshew and Radar criticised the lack of analysis of how 'Big Science' is 'big': 'this contrast is almost always implicit; small scale or 'Little Science' is usually defined as lacking one or another characteristic of Big Science, or as some vague historical predecessor' (Capshew and Radar 1992) (p. 3). Similarly, Robert Seidel commented:

The mobilization of science in World War II has often been taken as the origins of modern Big Science. This rests on the notion of 'Big Science' as a well-defined entity. An alternative view might be that Big Science, as we know it today, evolved more gradually over the course of the nineteenth and twentieth centuries (Seidel 1992) (p. 38).

### *1.5.2 (e) Characteristics of Big Science*

Four key characteristics are associated with Big Science: scale, social and political context, sponsorship and organisational issues.

#### *Scale*

Scale is a defining characteristic of Big Science: 'The drama of scale lies at the heart of our intuitions about Big Science, and, more generally, at the heart of scientific understanding and of our understanding of science' (Capshew and Radar 1992) (p. 18). The significance of scale extends beyond scientific necessity, and social and political issues can dictate the size of Big Science projects. For example, at the

Radiation Laboratory at the University of California in Berkeley,<sup>25</sup> the size of the cyclotron (a type of particle accelerator) was based on social and political issues rather than scientific ones: ‘the 60-inch cyclotron was oversized, a monument to megavolts and money’ (Seidel 1992) (p. 36). The significance of size is often related to the political importance of being the ‘biggest’:

The Crockfer Laboratory, which housed the 60 inch cyclotron, like the Lick Observatory, which housed the University’s [University of California in Berkeley] largest telescope, immortalized its patron, who was flattered by having the ‘world’s largest’ scientific instrument of this kind named after him (Seidel 1992) (p. 36).

Capshew and Radar have attributed the influence of Weinberg’s thesis to its focus on the scale of Big Science, highlighting the importance of scale as a characteristic. They claim that Weinberg’s thesis

entails a drama of scale that juxtaposes the huge machines, large organisations, and massive expenditures found in some contemporary research projects with the stereotyped lone investigator of the past, working with the proverbial sealing wax and string in a private laboratory (Capshew and Radar 1992) (p. 19).

### *Social and political context*

Big Science projects represent a convergence of politicians, journalists and scientists. The social and political context is reflected in demands placed upon scientists involved in Big Science to address a range of audiences in securing social and political support:

he must serve on committees that recommend who should receive support, who should not; he must travel to Washington either to advise a government agency or to cajole a reluctant contract administrator. In short, the research professor must be an operator as well as a scientist (Weinberg 1967) (p. 40).

Big Science projects rely on significant political and financial support, and as such depend on ‘the attachment of social and political significance ... whether for their

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<sup>25</sup>Later known as the Lawrence Berkeley Laboratory, the Radiation Laboratory was founded in 1931 at the University of California, Berkeley by Ernest Lawrence to develop physics research and was a national and international centre of nuclear science (Seidel 1992).

contribution to national health, military power, industrial potential, or prestige' (Hevly 1992) (p. 357).

The social and political context of Big Science is reflected in the changing position of the scientist and Galison has argued that Big Science entails 'a change in the very nature of a life in science' (Galison 1992) (p. 1). As their social and political responsibilities grew, scientists evolved into political instruments responsible for issues of national significance, such as defence or disease prevention. Price stressed the change to the role of scientists wrought by Big Science:

In the old days of Little Science there was tremendous reaction against political action by scientists. They were lone wolves; they valued their independence... Their pay-off was the approbation of peers, and they were not supposed to crave any sort of admiration from the man in the street or any social status within society. Whether they like it or not, they now have such status and an increasing degree of affluence (Price 1963) (p. 113).

Scientists' involved in Big Science projects bear such social and political responsibilities on account of the significance and potential benefits for society of their projects:

Society is supporting this structure and paying for it more and more because the results of his [the scientist's] work are vital for the strength, security, and public welfare of all. With everything said to be depending on him, from freedom from military attack to freedom from disease, the scientist now holds the purse-strings of the entire state (Price 1963) (p. 111).

Big Science projects also rendered scientists more accountable. This change was partly prompted by the perception that Big Science represented an ethical problem for society and science, following the bombing of Japan in the Second World War. Changes to institutional norms wrought by Big Science, such as scale and multiple authorship of scientific papers, challenged scientists' accountability. Capshew and Radar point to the difficulty of laying blame in the Challenger Space Shuttle disaster as evidence of the lack of accountability in Big Science projects (Capshew and Radar 1992).

Political support is a significant factor in the viability of Big Science projects and an intrinsic part of the wider context of Big Science. Scientists involved in Big Science projects must achieve political as well as scientific approval. For example, political acceptance was at the forefront of scientific decisions in the development of the Space Telescope: ‘the telescope’s designs, the program to build it, and the claims made on its behalf continually had to be revised and refashioned as part of the effort to come up with a telescope that would be politically feasible’ (Smith 1989) (p. 374). Scientific interests were however just as carefully balanced to retain astronomers’ support: ‘if the agency went too far in making cuts and thereby reduced scientific performance to a level the astronomers judged unacceptable, the telescope would be just as dead as if it had died at the hands of Congress’ (Smith 1989) (p. 374). Such is the political significance of Big Science that some scientists align their projects with the term to secure political support. However it must be carefully adopted, as Big Science is politically sensitive and can divide opinion. For example, the notion of Big Science was used and then rejected in justifying the HGP:

James Watson, the former head of the Human Genome Initiative, first argued that the project to map the human genetic structure was an appropriate extension of Big Science into the realm of biology...Recently, however, Watson has recognized the political liabilities in the analogy and has begun to speak of the genome project as taking a “Little Science” approach, partly because only the management and not the work itself will be centralized (Capsheew and Radar 1992) (p. 14).

The HGP represented a politically sensitive Big Science project because of its cost, the issue of access to the information, and public concern about the field. As a commercial company, Celera Genomics, rivalled the publicly funded effort to map and sequence the human genome, access to the human genome sequence was the most politically sensitive issue. It has been argued that the fear of a commercial company controlling access to the human genome sequence motivated the Wellcome Trust to double the funding for the British group to complete one third of the human genome:

Once the governors understood that Craig Venter’s [head of Celera Genomics] initiative was essentially a privatization of the genome, Michael Morgan [a representative of the Wellcome Trust] felt there was no risk that they would pull out on us (Sulston and Ferry 2002) (p. 163).

The political significance of the HGP was such that the completion of the first draft was announced in a press release involving the then Prime Minister Tony Blair and President Bill Clinton, a presentation perceived as a political gesture:

Of course, the 26 June announcement was a political gesture...It didn't matter that it was founded on the White House desire to get Al Gore elected. What mattered was that people were not talking about 'the race' anything like so much (Sulston and Ferry 2002) (p. 225).

Criticism of publicly funded science resulted in questionable Congressional support for the publicly funded HGP in the United States, which reflects the significance of political support for Big Science projects. For example, Sulston recalled how

[a]t the Sanger Centre [genome sequencing centre at Hinxton, Cambridge] we had the luxury of knowing that we had a politically independent body, the Wellcome Trust, behind us all the way. But in the US, with a Republican Congress, Francis [Replaced Jim Watson as Head of NIH Genome Program] feared that any suggestion that the private sector could do a better job than government-funded labs was going to find a receptive audience (Sulston and Ferry 2002) (p. 161).

### *Sponsorship*

Some regard the financial support required for Big Science projects as a definitive characteristic, setting it apart from other scientific projects. For example, Price said '[w]ithout doubt, the most abnormal thing in this age of Big Science is money. The finances of science seem highly irregular...they dominate most of the social and political implications' (Price 1963) (p. 92). Weinberg also regarded the cost involved in Big Science as highly influential on the nature of scientific studies: 'to what extent are the directions of science influenced by the availability of money rather than interest and promise of a field' (Weinberg 1967) (p. 40). Price argued that scientists' greater financial and social status, because of the costs involved in Big Science, changed the way in which scientists were judged by peers (Price 1963). Scientists' increased involvement in social and political issues is also attributed to the financial support required from government, industry or the military: 'Whether Big Science derives its support from designing patents, working for industry, contracting to the federal government, or building weapons, the demands of the wider society cannot be

ignored' (Galison 1992) (p. 2). Government, industrial and military sponsorship thereby reflect the wider social and political context of Big Science. This is evident in sponsors' motivations to support Big Science projects that extend beyond scientific validity. For example, economic and international factors motivated the White House and Congress to fund the Space Telescope:

to promote international ties, to strengthen the scientific/technological base of the United States, to help maintain the capability of the Marshall Space Flight Center, to provide employment in the districts and states of many congressmen and senators, and as part of a major initiative in the Ford presidency to promote the development of basic research (Smith 1989) (p. 387).

Given the considerable support required for Big Science projects, the relationships between scientists and their sponsors are significant, such that they 'became part of the intellectual and social context of Big Science' (Hevly 1992) (p. 359). Hevly parallels the influence of sponsors in Big Science projects to the increasing amount of sponsored research in the history of science:

the teams of historians may come to resemble, in miniature at least, the teams of scientists under study ... Scholars engaged in such projects should remain sensitive to the impact of these arrangements on our own work – arrangements that could influence the choice of topics, modes of presentation, and training of students (Hevly 1992) (p. 363).

Government is a significant sponsor of Big Science and their response to Big Science projects reflects wider issues surrounding scientific research funding. These issues were reflected in the U.K. in the MRC's approach to coordinating research on AIDS, and in the U.S. in attitudes to the publicly funded effort to sequence the human genome. Within the MRC, the traditional, responsive mode of research funding was changed in 1986 by the MRC Directed Programme on AIDS, which reflected increasing adoption of the 'customer/contractor' principle:

AIDS thus exemplified a tendency established in government funding of research with the Rothschild customer/contractor reforms of the 1970s, which stressed the production of research 'useful' to policy rather than the reactive mode of funded research which had previously prevailed (Berridge 1994) (p. 139).

Although this change was temporary, its influence is reflected in the adoption of the customer/contractor principle in the HGP: ‘The responsive mode of MRC funding was not, so it was argued, fundamentally altered by AIDS; only the human genome programme adopted some aspects of the AIDS Directed Programme model’ (Berridge 1994) (p. 144).

In the US, the HGP reflected tension between commercial and federal funded research. Lack of political support for publicly funded science meant that the NIH was under pressure to justify its involvement:

Healy’s [Director of NIH] gaze fixed on the commercial promise of genome research and the increasingly strong mandate to NIH from Congress and the administration to make science into technology and economic power. Watson [Head of NIH Genome Program] was determined to prevent a genetic gold rush that could undermine collaboration among research groups (Cook-Deegan 1994) (p. 326).

Such was the lack of Congressional support for publicly funded science that the NIH’s role was under threat, which rendered British involvement, free from private sponsorship, significant. For example, Sulston remarked that ‘[i]f the HGP had been just an internal US matter, then, with enough support for Celera in Congress I feared that the role and views of the National Institutes of Health might have been suppressed’ (Sulston and Ferry 2002) (p. 188).

Industry is also a prolific sponsor of Big Science, further reflecting its wider social and political context. The significant role of industry in Big Science is evident in the involvement of the commercial company, Celera Genomics, in the HGP. Venter’s attempt to sequence the human genome faster threatened scientists within the publicly funded effort as they feared that their public sponsors would not continue to fund an initiative that had private support (Sulston and Ferry 2002). The tension surrounding the involvement of Celera Genomics largely concerned access, specifically the idea that the human genome sequence would not be freely available public information. It is argued that involvement of a commercial company in the HGP and their restrictions on access were indicative of shifts in the ‘prevailing ethos in the world of science’ regarding access and data sharing:

What was once a collective enterprise, in which discoveries were acknowledged but their results freely shared, is now frequently constrained by the demands of commercial competition. Motivated by financial gain, hamstrung by sponsorship deals, or simply out of self-defence, many researchers trade their discoveries with the rest of the community only under the protection of patent law or commercial secrecy (Sulston and Ferry 2002) (p. ix).

Given the resources involved, scientists increasingly accept the role of industry in sponsoring Big Science projects. However, some scientists reject the assumption that industry involvement is essential in Big Science projects. For example, Sulston commented that '[t]he success of the Sanger Centre and the other big genome labs have shown that size is not an issue: the often-heard notion that only industry can handle large-scale science is incorrect' (Sulston and Ferry 2002) (p. 273). Scientists warn of the pressures placed on academics from industry: 'all universities now hold contracts with industrial sponsors out of sheer necessity; the question is to what extent the sponsors thereby gain control over what is and what is not discovered' (Sulston and Ferry 2002) (p. 273). Industry involvement in Big Science can therefore result in tension between academic scientists and industrial sponsors. This tension is evident in the HGP in Sulston's criticism of Craig Venter's behaviour as unscientific and business-like:

He had certainly opened up a huge public relations advantage...it's a skill that most scientists never learn and rarely have to practice. The convention is that you don't announce anything until the work is completed and accepted for publication in a peer-reviewed journal ... But Craig was no longer in science, he was in business. And the priority for a business is not scientific credibility but share price and market penetration (Sulston and Ferry 2002) (p. 159).

### *Organisational Issues*

Big Science projects are characterised by large, multidisciplinary teams and hierarchical organisations. They involve the establishment of specialist research groups with particular goals in mind (Hevly 1992). Increasing specialisation is not however restricted to scientific enterprise and is reflected in organisational structures: 'Laboratories have been divided not only into groups of theoreticians, experimenters,



and instrument builders, but also into hierarchies of group leaders, laboratory managers, and business coordinators' (Hevly 1992) (p. 357). Such centralised organisational structures, typical of Big Science, are at odds with those traditionally favoured by scientists. It is argued that criticism of Big Science represents criticism of centralisation: 'Many scientists dislike Big Science because it can mean a loss of autonomy through a centralization of decision making' (Smith 1989) (p. 379). Smith referred to astronomers' experience of a centralised structure in the development of the Space Telescope in demonstrating criticism of centralisation: 'For some astronomers, immersion in the highly ordered and hierarchical world of the Space Telescope was, on occasion, an uncomfortable and demoralizing experience' (Smith 1989) (p. 380).

The role of scientific champion is a significant aspect of the organisational structure of Big Science. Increased scrutiny from sponsors in Big Science projects, such as government, renders the role of scientific champion especially important: 'any proposed project must have advocates in the scientific community who are willing to work to mobilize its supporters, argue with doubters, and spend much time on advisory committees' (Smith 1989) (p. 375). The responsibility for garnering political and financial support rests with the scientific champion, which is significant given the social and political context of Big Science.

Given the involvement of multiple stakeholders in Big Science, control can be a significant issue in organisational structures, which is reflected in tension between scientists and the funding bodies. Such tensions are evident in the development of the Space Telescope (Smith 1989). Doubting NASA's long term commitment, astronomers outside of NASA supported the establishment of the Space Telescope Science Institute as they perceived it as a means to increase their control over the telescope. Following astronomers' complaints that the Science Working Group was 'toothless' on account of its role, infrequency of meetings and large size, NASA established The Space Telescope Observatory Performance and Assessment Team (STOPAT) (Smith 1989) (p. 318).

The origins of CERN further illustrate tensions over control, in this case between European states and CERN officials. European states' reluctance to become involved

in CERN was attributed to their lack of control over it: ‘many states hesitated about getting involved in a business whose long-term development was difficult to foresee and which they did not control’ (Pestre and Krige 1992) (p. 82). Tension persisted between the CERN Council and state authorities, resulting in the Council adopting a powerful position of control, supported by a close relationship with the European high-energy physics community. Such was their control that the Council ‘was not only the organ representing the states and responsible for *controlling* CERN, but also the body expected to *advise* the same states on matters concerning CERN and high-energy physics’ (Pestre and Krige 1992) (p. 86).

Different organisational styles can also result in tension in Big Science projects, such as perceptions of organisational approaches as academic and non-academic. Gowing associated academic or university principles in organisational structures with debate and scientific autonomy. For example, she described how the British Atomic Energy institution at Harwell [a research establishment led by John Cockroft] represented academic practice:

all work, whatever its purpose, was done in accordance with academic traditions – that is, endless debate without closure motions, the reopening of decisions that had been taken, and the absence of coercion on staff to change their approach or their work (Gowing 1974) (p. 14).

Gowing distinguished this academic approach undertaken at Harwell from those of the two other institutions and their executives in the British Atomic Energy Project, which were described as non-academic:

Penny [responsible for making and testing an atomic bomb at the Ministry of Supply’s Armament Research Department] and Hinton [responsible for the design, construction and operation of four large plants to produce fissile material] on the other hand had to organise the whole work of their establishments to meet very tight deadlines; there had to be strong command and pyramid-shaped hierarchies. There could not be perpetual debate or a refusal to regard any issue as finally decided (Gowing 1974) (p. 16).

### 1.5.2 (f) *Criticisms of Big Science*

Scientists criticise Big Science on various grounds, including its social and political context, cost and organisational structure. Weinberg's comments reflect this range of criticism directed at Big Science projects:

I have inveighed against the dangers of Big Science: its too-frequent preoccupation with the big announcement rather than the big discovery, its tendency to substitute money for thought, its overabundance of administrators, its incompatibility with the educational process, even its inefficiency (Weinberg 1967) (p. 113).

The following analysis of criticisms of Big Science reflects many of those directed at UK Biobank, which will be addressed in the findings chapters.

Criticisms of the cost of Big Science not only concern the sums of money involved but the effect on other research activities of committing significant sums to a single project. For example, astronomers felt that the costs involved in operating, maintaining and refurbishing the Space Telescope threatened other space science programs: 'NASA was driven to siphon money away from potential new space science programs to shore up the Space Telescope's budget. One mission to suffer was the Advanced X-Ray Astronomy Facility (AXAF)' (Smith 1989) (p. 395). Similarly, scientists argued that the funding of the HGP would be to the detriment of biological research funding: 'The new band of dissidents were troubled, even angered, by the fact that, while the genome project had been prospering, general basic research in the biological sciences had been financially squeezed' (Kevles and Hood 1992) (p. 301).

Industrial sponsorship attracted further criticism for Big Science, and some scientists, such as Paul Zilsel in 1964, argued that it denoted 'the triumph of the values of big business in science' and portrayed Big Science as 'a market-conscious, product-orientated, and capital-intensive activity' (Capsheew and Radar 1992) (p. 10). Criticism of the costs involved in the HGP reflected fears that its funding was indicative of the lack of funds for small, independent grants:

scientists supported by small independent grants felt squeezed...dissension was palpable among the reviewers... the central issue was not the genome

project *per se*, but the paucity of investigator-initiated project grants (Cook-Deegan 1994) (p. 171).

Organisational issues are a further source of criticism of Big Science, specifically distrust of large centralised operations. Weinberg criticized group activity as less conducive to creative science and problem solving than individual effort: ‘Growth and fragmentation impair the efficiency of science by forcing science to become a team activity ... The act of scientific creation, no less than any intellectual creation, is largely an individual act’ (Weinberg 1967) (p. 43). In the HGP, scientists were suspicious of overt state control: ‘In France, molecular biologists were particularly resistant to bigness and centralization ... Most preferred the model of the Institut Pasteur, a private institution that had long insulated itself from state control’ (Kevles 1992) (p. 29).

Big Science therefore represents a highly emotive phenomenon, which incurs strong reactions from scientists. This emotive nature is reflected in perceptions of the HGP as a Big Science project. Some scientists’ criticised the Project simply for representing Big Science. They feared that it signalled the beginning of ‘big biology’: ‘the renewed criticism of the project echoed, in part, the main animadversion cast upon it in 1987 – that it represented the subjugation of biology to the directed, hierarchical mode of Big Science’ (Kevles and Hood 1992) (p. 301). Criticism of the HGP also concerned its lack of hypothesis, which can be a characteristic of Big Science: provision of resources for as yet unspecified future research. Martin Rechsteiner, a Professor of biochemistry, criticised the project on these grounds:

Rechsteiner held that ascertaining the sequence even of coding regions would not necessarily advance biological science: the effort would obtain DNA data for the sake of acquiring the information, independent of hypotheses that the data might address (Kevles and Hood 1992) (p. 301).

Such was the potency of criticism of the HGP for representing Big Science that it partly overshadowed criticism of other aspects of the project, such as access and data sharing (Kevles 1992). In the US, descriptions of the HGP as a Big Science project were both detrimental and beneficial to perceptions of the Project. It is argued that the association between the HGP and Big Science was made selectively to foster criticism

and reflects singular definitions of Big Science that are detrimental to understandings of it:

Unfortunately, the way that the genome project has been identified with Big Science in scientific journals and the press has tended to cloud matters. The distinction has been selective ... the genome project is a type of Big Science, but it is not the type that its critics deplore (Kevles and Hood 1992) (p. 306).

However in the US, the association of the HGP with Big Science partly accounted for the DOE's support, which helped prompt the NIH to become involved (Kevles 1992). Some biomedical scientists were so suspicious of the DOE that they urged the NIH to get involved in the HGP simply to limit their power. Despite the NIH's increasing commitment to the genome project, biomedical scientists continued to object to the endeavour on account of its Big Science status:

The project might now be largely in the friendly hands of NIH, but it suffered from the image that Walter Gilbert [an early proponent of the project] had given it – a three-billion-dollar Big Science crash program, built around a few large, bureaucratized centers that would be given over to DNA sequencing and accomplish their task within several years. The work would be tedious, routinized, and intellectually unrewarding, the critics contended. In their view, sequencing the entire human genome would amount to bad and wasteful science (Kevles 1992) (p. 24).

### 1.5.3 Concluding Remarks

This literature review has enabled a greater understanding of the origins and development of UK Biobank. First, analysis of the historiography of contemporary science fostered my awareness of the methodological issues involved in undertaking a contemporary history of the origins and development of UK Biobank. It allowed me to understand interviewees' reactions to my research more fully, and increased my awareness of the meaning behind them. Second, in reviewing the term Big Science and the origins and development of such projects, I increased my understanding of the phenomenon, which will enable a more full consideration of the extent to which UK Biobank represents Big Science in the conclusion.

The issues raised throughout the literature review are reflected in my research. For example, I encountered difficulties in handling scientists' perceptions of the role of contemporary history, which are addressed in chapter three. The organisational issues, characteristic of Big Science and a source of criticism, are especially relevant to my study. For example, I found that the role of scientific champion and the issue of centralisation that are considered in the findings chapters four and five were significant in the origins and development of UK Biobank. For the remainder of this chapter, I will provide a brief outline of the thesis.

## 1.6 Thesis Outline

In Chapter two I discuss the methods adopted in researching the origins and development of UK Biobank, including the theoretical and practical issues encountered in employing oral history interviews and archival research. I address the advantages and disadvantages of the methods and describe how I analysed the data from the oral history interviews and archival research. Chapter three therefore represents a reflexive account of my experience of gathering the data that supported my findings and informed my conclusions. It allows the reader to understand how I conducted my study, analysed the data and subsequently formed findings and conclusions.

Chapter three presents a detailed chronology of UK Biobank, largely based on information gathered from archival research and the UK Biobank website. The chapter is descriptive in nature rather than analytical, and serves to familiarise the reader with the evolution of UK Biobank and the terminology surrounding it.

I present my findings in chapters four, five and six. Chapter four discusses the issue of ‘standard academic scientific practice’. Specifically this chapter details how members of the academic scientific community saw the way in which UK Biobank was established as representing a departure from standard academic scientific practice. It also examines understandings of standard academic scientific practice, the nature of the meanings attached to it, and the perceived consequences of departure from this model of science. Chapter five concerns the confusion surrounding control of UK Biobank, which was responsible for much tension between academic scientists on the one hand and representatives of the funding bodies and UK Biobank Limited on the other. It focuses on perceptions of where control of UK Biobank lay, explanations for the confusion regarding control, and perceptions of the organisational changes as resolving confusion over control. Chapter six examines the lack of trust between academic scientists, representatives of UK Biobank Limited and the funding bodies in the origins and development of UK Biobank. It described how members of the academic scientific community felt that the funding bodies and UK Biobank Limited did not trust them to develop the resource. In turn, academic scientists felt that they could not then trust the funding bodies to develop UK Biobank. This chapter analyses

such perceptions of a lack of trust and explanations for it, focusing on the ways in which the lack of trust manifested.

Chapter seven is an evaluation of my study that begins with a summary of the thesis. I discuss my findings in the wider context of Big Science, specifically by examining how UK Biobank could be regarded as a Big Science initiative and comparing its origins and development to that of other Big Science projects. This chapter also includes discussion of possible explanations for the selection of some of the most controversial aspects of the organisational structure that were not documented. I present my conclusions regarding the organisational issues that shaped the configuration of UK Biobank and reflect upon the strengths and limitations of my research, before finally considering potential future directions of this research.



## **Chapter 2**

### **Methods**

#### **2.1 Introduction**

In this chapter I will discuss the methods I employed in researching the origins and development of UK Biobank from its inception until the organisational changes in August 2005. However, because of the organisational changes that occurred unexpectedly toward the end of my fieldwork period, I had to extend my period of fieldwork until March 2006. First of all, I address issues surrounding the terminology I use. Second, I will discuss the theoretical issues involved in conducting a historical study, focussing particularly on oral history. Third, I describe my experience in conducting oral history interviews and archival research, reflecting on the pros and cons of the methods. Last, I will report on how I analysed the data from the oral history interviews and archival research.

#### *Terminology*

Throughout my fieldwork, the terminology relating to UK Biobank was an important issue although I was not aware of the sensitivities surrounding the terminology when I began my fieldwork. This sometimes led to confusion in my questioning, and annoyance from interviewees, particularly current committee members and representatives of the funding bodies. Sensitivities regarding terminology concerned reference to UK Biobank as a ‘project’ or a ‘study’, description of UK Biobank as a ‘genetic study’, and reference to the ‘spokes’ and ‘hub’ as ‘Regional Collaborating Centres’ (RCCs) and the ‘Central Coordinating Centre’ (CCC).

Description of UK Biobank as a ‘project’ or a ‘study’ rather than a ‘resource’ was a key issue. For example, a member of the IAG in response to the question ‘Where do you think the initial idea for the study came from?’ remarked:

I sermonise everybody that Biobank is not a study, it should not be referred to as a study....it is not going to do any studies...’Resource’ is probably the best word for it...Studies are research, have research protocol and they have an objective to study a particular thing and Biobank is going to be a multi-

purpose resource...I'm sorry for saying that to you but it's just something for you to think about [090; p. 123; p. 3].

Thereafter, I made a conscious effort to refer to UK Biobank as a 'resource', 'endeavour' or 'initiative'. Throughout this thesis, I only refer to UK Biobank in these terms. Such sensitivities reflected underlying tensions surrounding the nature of UK Biobank itself. For example, some members of the academic scientific community criticised the initiative for a lack of hypothesis, and representatives of the funding bodies and UK Biobank Limited defended UK Biobank against this criticism by arguing that it was not a study, but a resource that would address a range of hypotheses.

I also encountered adverse reactions to my description in the information sheet of UK Biobank as a 'genetic study'. Representatives of UK Biobank Limited and the funding bodies were sensitive to such a description and stressed that it was not solely a study that involved genetics. For example, when asked if he had any questions, a representative of UK Biobank Limited remarked:

I noticed in your information sheet you call it a big genetic study or whatever but, you know, just to highlight that so many people refer to it as that but it is so much more than that and in fact, it has probably been pointed out to you already, but DNA might well not be looked at from all participants and certainly not everybody could have their DNA analysed and not every bit of their DNA is going to be analysed even if it was ... People find it 'sexy' to say 'It's the biggest genetic project' or it is DNA focussed but it is not just that and we are keen to emphasise that that it not just what it is about because people get the wrong impression of us [0602; p. 186; p. 4].

His concerns revealed the controversy surrounding genetic research, and UK Biobank Limited's efforts to avoid it. For example, he continued:

Not everybody is going to have DNA analysis done and when you talk about DNA and genetics for some people it seems scary, you know, genetics equals scary and all that sort of thing, slippery slope, genetic underclass and all that sort of business...there are some ethical concerns around about that but people seem to conflate our project, UK Biobank, with other projects like the National DNA Database and the Forensic DNA Database [0602; p. 186; p. 7].

As these concerns came from a minority of interviewees who represented just two groups in the sample, I did not amend my information sheet in accordance with their views.

During the earlier stages of my research the terminology regarding the organisational structure was changed. For example, the ‘spokes’ became ‘RCCs’ and the ‘hub’ became the ‘CCC’. The extent to which these terms were adopted varied across the sample and within constituent groups. In general, representatives of UK Biobank Limited and the funding bodies consciously adopted the latter terms, but those associated with the origins of the initiative continued using the former terms. Some representatives of the academic scientific community used the terms whereas others did not adopt them. Often interviewees from all constituencies would use the terms interchangeably. To avoid confusion and as my research concerned the origins and development of UK Biobank, I use the terms ‘spokes’ and ‘hub’ rather than ‘RCCs’ and ‘CCC’ throughout the thesis except in direct quotations from interviewees or archival documents.

## 2.2 Historical Theory

### *Introduction*

Historical theory is surrounded by a number of debates;<sup>26</sup> I will provide a brief overview of these beginning with discussion of empiricism, relativism and postmodernism in relation to historical methodology. I will then focus on the theoretical issues involved in oral history, as the chief method employed in my research. Last, I address why I selected oral history interviews and archival research in my study of the origins and development of UK Biobank.

Empiricism is understood as representing the ‘search for objective truth’. It was the most important theoretical position in historical study. For example, Anna Green and Kathleen Troup describe it as ‘without doubt the most influential school of historical thought over the course of the century’ (Green and Troup 1999) ( p. 1). Empiricism was related to the theory of positivism, which was influential across the social sciences. Its influence was responsible for the dominance of archival research as a historical method to the detriment of other methods and sources, such as oral sources, personal memoirs and accounts written after the event. Historians considered analysis of written documents as the only reliable means to gather factual evidence and access objective truth. Empiricism was challenged by the theory of relativism and postmodernism. According to the relativist tradition, it is not possible to attain absolute truth, and the position of the historian is relative to any statements about history. The relativist position stresses the role of the historian in interpreting data and hence the importance of assessing his or her influence on the research. For example, Edward Carr remarked that ‘when we take up a work of history, our first concern should be not with the facts which it contains but with the historian who wrote it (Carr 1988) (p. 22). Postmodernists also stress the significance of the historian’s role in research and argue that historical research is the product of the historian’s perspective rather than any fixed truth. Postmodernism challenges traditional understandings of archival research as it argues that historical documents only represent one understanding of reality, further rejecting the idea of a single truth.

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<sup>26</sup>For an introduction to these debates see (Green and Troup 1999)

Given the various notions of truth that emerged from these traditions, the reliability of archival research was questioned and attention focussed on the construction and preservation of documents (Thompson 2000) (p. 97). Relativist and postmodernist challenges to empiricism also led to a new emphasis on other historical methods, particularly oral history. I will now focus on the implications of the trend towards relativism and postmodernism on oral history, including a comparison of the theoretical issues facing oral history and archival research as they relate to my research.

### 2.2.1 Oral History

Oral history underwent a revival of interest in the 1960s characterised by the politics of the New Left, civil rights and feminism. Historians sought to access the experiences and opinions of underrepresented groups, such as women, working classes and ethnic minorities. They felt that these groups were underrepresented due to reliance on archival research and perceived oral history as a ‘means to empower’ them (Green and Troup 1999) (p. 231).

Oral history was criticised by advocates of the empiricist tradition for being unreliable and subjective due to its reliance on memory. It was perceived as an inadequate method for gathering factual evidence. For example, Eric Hobsbawm described oral history as ‘a remarkably slippery medium for preserving facts’ (Hobsbawm 1997) (p. 206). As relativism and postmodernism became more influential, this subjectivity began to be perceived as a strength of the method, rather than a weakness. Oral historians argued that understanding of the meanings behind subjective evidence in oral sources resulted in richer understandings. For example, Luisa Passerini concluded that oral testimonies are ‘pre-eminently an expression and representation of culture, and therefore include not only literal narrations but also the dimensions of memory, ideology and subconscious desires’ (Passerini 1979) (p. 84). This emphasis on the credibility of subjective evidence was accompanied by a focus on the role of the historian to understand representations of the ‘truth’ in oral testimonies, specifically how and for what purpose the data are true (Green and Troup 1999) (p. 236). This period was described by Michael Roper as ‘oral history in the interpretive model’ (Roper 1996) (p. 347).

### *Oral History and Memory*

As discussed, the key criticism of oral history is its reliance on memory in constructing accounts. Oral historians argue that these problems are lessened when the topic is of interest or relevance to the interviewee. For example, Paul Thompson remarked that '[t]he memory process thus depends, not only upon individual comprehension, but also upon interest. Accurate memory is thus much more likely when it meets a social interest and need' (Thompson 2000) (p. 103).

Oral historians argue that understanding of the process of memory making can not only overcome the problems associated with memory, but can offer fuller insight into issues. In constructing accounts of the past, it is believed that people alter the way in which events occurred to comply with an overall narrative. Oral historians relate this need to construct a coherent account to the concept of 'composure' (Green and Troup 1999) (p. 234). Composure describes the process of memory making and is the theory that memories are constructed in accordance with the language and meanings of our culture, and personal accounts are constructed to correspond with our personal identity and make us feel comfortable with our lives. For example, Alistair Thomson states:

[w]e compose our memories so that they will fit with what is publicly acceptable, or, if we have been excluded from general public acceptance, we seek out particular publics which affirm our identities and the way we want to remember our lives (Thomson 1999) (p. 241).

It is believed that the influence of present identity in constructing accounts of the past is greater the further back in time the interview goes. For example, Thompson states that

[t]he information provided by interview evidence of relatively recent events, or current situations, can be assumed to lie somewhere between the actual social behaviour and the social expectations or norms of the time. With interviews which go back much further, there is the added possibility of distortions influenced by subsequent changes in values and norms, which may perhaps quite unconsciously alter perceptions (Thompson 2000) (p.100).

Oral historians argue that oral sources offer a rich understanding as they allow historians to access the effect of present identity on memory making and perceptions of the past. Oral sources are therefore useful for offering greater insight into the past through evaluation of the influence of the present. The effect of societal changes in accepted norms of behaviour and opinions on the construction of personal accounts of the past can also be revealed in what interviewees do not say. As Alessandro Portelli states ‘the specific utility of oral sources for the historian lies, not so much in their ability to preserve the past, as in the very changes wrought by memory’ (Portelli 2003) (p. 69).

Critics point to discrepancies between what is recorded in written documents and what is said in an oral history interview as a result of how memories are constructed. Some oral historians interpret these discrepancies positively, and argue that investigation into why there is a discrepancy offers greater insight into a particular issue. For example, Portelli interprets factually incorrect accounts (in his example, the date of the death of a famous protestor) ‘not as the product of faulty memory, but as an active creation which gives us insight into the way in which experience is symbolically and psychologically incorporated into memory’ (Green and Troup 1999) (p. 234). Oral historians also point to the fact that oral accounts are constructed in the present to further explain the reasons for discrepancies between written documents and oral sources. I encountered discrepancies between archival research and oral history interviews in my research, and would agree that investigation into their nature offered greater understanding and reflected the importance of present identity in constructing accounts of the past.

#### *The Role of the Oral Historian in the Interview*

Oral historians stress the importance of assessing the influence of the historian on the content of the interview. An interesting part of this debate, which is relevant to my research, is the significance of a historian representing an insider or an outsider. Qualitative literature offers valuable insights into the effect of the researcher on the interview interaction, which I will briefly explore. The historian’s position as an insider or an outsider and his or her professional and personal characteristics were especially important issues in my research as I interviewed elite groups (see 2.3.9).

On the one hand, some argue that being an insider or a member of the group is a privileged position as you have a greater knowledge of the issue and people involved. It is believed that group membership allows the researcher to access information unobtainable to those not familiar with the culture of the group, especially regarding sensitive or controversial issues. On the other hand, in being an insider there is the danger of conformity, as Thompson states: 'If the social relationship in an interview becomes, or is from the start, a social bond, the danger towards social conformity in replies is increased. Nor does increased intimacy always bring less inhibition' (Thompson 2000) (p. 116). An outsider is less familiar with the group and the issue at stake, but this can be advantageous as the researcher may be less inhibited and less afraid to ask 'obvious' questions, whereas the insider could be guilty of assuming answers (Thompson 2000). It is argued that an outsider can adopt a more neutral position and perhaps achieve a fuller understanding than a group member. As each interview is different and each position has its merits, it is argued that as long as the influence of the historian is assessed and neither position is assumed to be privileged the issue is not critical. For example, Akemi Kikumura states

[s]ince both perspectives have the possibility of distortions and preconceptions of social reality, it is the role of the researcher to evaluate the distinctive advantages and limitations of each perspective in relationship to the problem of research at hand' (Kikumura 2003) (p. 141).

In my research, I occupied the position of an outsider in conducting oral history interviews and found that it had advantages and disadvantages, which I will address in 2.3.9.

The influence of the researcher's professional background and personal characteristics on the interview is a key debate in sociological literature.<sup>27</sup> One interesting example of this debate is provided by Helen Richards and Carol Emslie who found that the respondent's perceptions of the researcher, in their case as a general practitioner and sociologist respectively, influenced their response and therefore the interview interaction. For example,

Doctors have a more clearly defined role and higher social status than sociologists. This difference in status led to the more frequent observation by

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<sup>27</sup> For a discussion of this debate see: (Altheide and Johnson 1994), (Ambert, Adler et al. 1995), (Hoddinott and Pill 1997), (Morgan 1986)



HR [Helen Richards] than CE [Carol Emslie] of deference amongst working-class respondents and social alignment amongst middle-class respondents (Richards and Emslie 2000) ( p. 6).

Social scientists argue that researchers must be aware of the significance of an interviewee's preconceptions of their professional background. They stress that researchers must address these preconceptions regardless of whether or not their professional roles are clearly defined. For example:

[GP researchers] should be aware of respondents' possible preconceptions and take care to explain their current role as researcher. Sociologists and other social scientists, who have less a clearly defined professional role and status, face the similar challenge of making their professional background and interests clear' (Richards and Emslie 2000) (p. 7).

The effect of the researcher's personal characteristics (such as gender and age) as well as professional background on the interview can be significant: 'The GP's perceived higher status led to obscuring of her personal characteristics. The sociologist was often perceived as a 'young woman' rather than defined by her professional role' (Richards and Emslie 2000) (p. 2). I will explore the effect of my professional and personal characteristics on the interview interaction, particularly in relation to researching elites, in 2.3.9.

### *Oral History and Archival Research*

Oral historians argue that archival research and oral history share similar characteristics and in terms of reliability they should each be treated with caution. In exploring these characteristics, I will focus on the following issues that are relevant to my research: the accuracy of oral sources compared to written documents and the role of the historian in oral history and archival research.

Some oral historians argue that a key difference between written and oral sources is the way that they are presented. They point to how oral sources present themselves in an oral form, and in a recorded form represent the words used exactly and offer other insights by way of pauses and humour. By contrast some written documents, such as the official minutes of meetings, record what the scribe believed happened or wished to record, rather than exactly what happened (Thompson 2000) (p. 98). For example, the historian David Edge, in conducting research into the development of radio

astronomy, found that the records preserved by the scientists involved were not indicative of the issues that marked the history of radio astronomy. He knew that the records did not represent the full story as he was also involved, and following oral history interviews with the scientists involved he gained understanding of these issues. Thompson argues that through oral history interviews

he [David Edge] has been able to show that the true picture is very different: a story of dead-ends, of misunderstandings, and of discoveries by accident, within a social setting of acute rivalries, partly handled by group specialization, but sometimes leading to the deliberate concealment of information (Thompson 2000) (p. 69).

Oral historians stress the extent to which oral sources share the same problems as written documents in terms of accuracy. For example, oral history is criticised for being distant from the events to which it refers. Oral historians point out that written documents tend to be written after the event and by people who did not take part in them directly; hence accuracy is as much a problem for the written source as the oral (Portelli 2003) (p. 68).

A feature distinguishing oral history and archival research is the role of the historian, which is more significant in oral history. It is argued that the written source is independent of the historian's hypothesis and can only be interpreted, whereas the content of oral source depends on the historian's role in the interview and their relationship with the interviewee (Portelli 2003) (p. 70). For example, the historian decides that he or she would like to conduct an interview with a particular person. The historian's age, gender or background can influence the interviewee and the content of the interview. For example, Portelli states how '[r]esearchers often introduce specific distortions: informants tell them what they believe they want to be told and thus reveal who they think the researcher is (Portelli 2003) (p. 71). Oral historians stress the importance of assessing this influence rather than trying to remove it to create neutrality.

### 2.2.2 Why oral history interviews and archival research?

My research aim was to understand the origins and development of UK Biobank and answer the following question: how and why was UK Biobank initially configured in

the manner it was? I sought to answer this question by gathering the opinions and experiences of those involved in the origins and development of the resource, specifically academic scientists, representatives of the funding bodies and representatives of UK Biobank Limited. I also choose archival analysis to address the question, thereby accessing different perspectives regarding the origins and development of UK Biobank.

I employed oral history interviews as I felt they were the most appropriate method for gathering the opinions and experiences of those involved in the origins and development of UK Biobank. The main reasons for conducting oral history interviews as opposed to using other qualitative methods such as focus groups<sup>28</sup> were the sensitivity of the research, the importance of confidentiality and the timing of the research. The controversy surrounding the timing and organisational structure of UK Biobank meant that my research into its origins and development was a sensitive project. It was therefore critical that respondents felt comfortable to share their opinions freely and the interview context provided a sufficiently safe environment. Interviewees' position within UK Biobank, particularly representatives of the funding bodies and senior members of the BoD, the Science Committee and spokes meant that they may have felt that involvement in my research could have been to the detriment of their career and involvement in UK Biobank, depending on their views. It was important that their involvement and responses were treated in the utmost confidence and this would have been impossible in a focus group setting. The timing of the research further contributed to the importance of confidentiality. As interviewees were commenting on recent and evolving events as well as past events, their position was particularly difficult, which further underlined the need for confidentiality. Although I was unable to conduct focus groups in my research primarily on account of the importance of protecting respondents' identities, the interaction between group participants would have been a useful addition to in-depth oral history interviews. Also, it would have been helpful to witness the ways in which participants refined their contributions in relation to each other, which is a key feature of focus groups (Lewis 2004).

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<sup>28</sup>For a discussion of focus groups see: (Barbour and Kitzinger 1999), (Bloor, Frankland et al. 2001), (Casey and Kleuger 2000), (Morgan 1997)

I adopted semi-structured, rather than structured or unstructured, interviews.<sup>29</sup> Semi-structured interviews were the most useful in my research as they involve pre-selected open-ended questions yet allow the interviewer and respondent to diverge from the schedule to explore issues further. Conducting semi-structured interviews allowed me to ask similar questions to every interviewee, and afforded me a certain amount of flexibility to tailor the interview to the respondent's specific experience and seek further explanation (Arskey and Knight 1999).

I choose archival research because I felt it would be a useful way to complement understanding of the themes that emerged from oral history interviews. I felt that the same episodes and issues documented in archival research, such as protocol development, would emerge in the oral history interviews. Archival research would thereby aid my understanding of such themes by supporting the data gathered in oral history interviews or offering different perspectives to it. I did however hope that the content of the official documents would correspond with the content of the interviews, and thereby validate the data generated in the oral history interview. I felt that correspondence between what respondents said in an interview and what they were reported to have said in a meeting regarding a particular issue (as documented in the minutes) would reinforce the validity of my methods. I consider the extent to which archival research corresponded with the data generated in oral history interviews in 2.4.3. I initially endeavoured to complete archival research prior to commencing oral history interviews, thereby using it to inform the interview schedule and find focus. Archival research was also selected to allow me to access different insights into the origins and development of UK Biobank that were not available through conducting oral history interviews. I felt that as the official documents were produced at the time, especially emails and written correspondence, they would offer a different understanding of the origins and development of UK Biobank than oral history interviews conducted after the events. I felt that access to official documents would allow me to gain access to a wider range of opinions, such as those of people who would not wish to be interviewed, or who occupied temporary but significant positions. As it would have been impossible to interview every person connected to the origins and development of UK Biobank, archival research gave me the opportunity to access

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<sup>29</sup>For a discussion of the different types of in-depth qualitative interviews see: (Fielding 2003), (Arskey and Knight 1999), (Bryman 2001), (Denzin and Lincoln 2000)

a wider range of opinions and experiences. I also felt that it would offer different insights in terms of the sensitivity of the issues; interviewees may have been reluctant to discuss controversial episodes but these may have been documented. Access to official documents enriched my overall understanding of the origins and development of UK Biobank as it allowed investigation of issues that were not part of my research and not explored in oral history interviews. Although these aspects were not investigated further they served to aid understanding of the wider issues. I also choose archival research as it allowed me to produce a meaningful chronology of events that was not connected to memory. This not only aided understanding of the origins and development of UK Biobank, but assisted greatly in understanding the interviewees' experiences and opinions.

## 2.3 Oral History Interviews

### 2.3.1 Sampling

#### *Sample Composition*

I conducted 76 oral history interviews; 64 were part of my main study and 12 were follow-up interviews (see table 1). I approached and interviewed representatives of the academic scientific community directly and indirectly involved in UK Biobank, representatives of all four funding bodies and representatives of UK Biobank Limited (also known as the hub)<sup>30</sup>. Interviews with representatives of the academic scientific community directly involved in UK Biobank included spoke members and current and previous committee members (specifically the Science Committee, the BoD, the EGC and the EWG, the PDC, and the IAG) (see table 1). Within these groups I targeted those representing a range of academic backgrounds, for example general practice, epidemiology, psychiatry, genetics and statistics. Interviews with representatives of the academic scientific community indirectly involved in UK Biobank included unsuccessful spoke bidders and members of the academic scientific community outside UK Biobank (critics and former spoke members). The 12 follow-up interviews were conducted with a sub-sample of the original participants in response to the organisational changes; specifically spoke members (a representative from each of the six spokes), representatives of the funding bodies, UK Biobank Limited and committee members (see table 1 ‘no. re-interviewed’).

For the main study, oral history interviews were conducted between October 2004 and September 2005 (see table 2). During this period of fieldwork, the hub and the spokes were still undergoing contract negotiation, the EGC was established (November 2004), the former CEO, John Newton, resigned (December 2004), the phase one pilot study was undertaken (February 2005), and Rory Collins was appointed as CEO and PI (August 2005). The follow-up interviews were conducted between January and March 2006 as the organisational changes that followed the appointment of Rory Collins unfolded. UK Biobank was therefore an evolving initiative, which created

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<sup>30</sup> See Appendix B9 for a list of the transcripts referred to in the thesis

particular methodological issues in researching its origins and development that are addressed in the following sub-sections.

Table 1: Sample Composition<sup>31</sup>

	Hub	Spokes	Science Comm.	EGC	BoD	IAG	PDC	EWG	Funders	Indirectly Involved	Male	Female	Total
No. Approached	6	43	9	5	5	4	9	8	10	11	64	25	89
No. Agreed	6	40	7	3	5	3	8	5	6	5	54	15	69
No. Interviewed	5	37	6	3	5	3	7	5	6	5	50	14	64
No. Taped	4	33	5	3	5	3	7	5	6	5	49	9	58
No. In-Person	5	23	5	2	3	1	6	5	5	2	32	10	42
No. Telephone	0	14	1	1	2	2	1	0	1	3	18	4	22
No. Re-interviewed	1	7	0	0	1	0	0	0	3	0	9	3	12

Table 2: Timing of Interviews

	Hub	Spokes	Science Comm.	EGC	BoD	IAG	PDC	EWG	Funders	Indirectly Involved	Total
Oct-Dec 2004	1	11	4	1	1	1	3	1	0	0	14
Jan-Mar 2005	0	6	2	0	4	0	3	2	4	0	15
April-June 2005	4	15	0	2	0	2	1	2	2	3	29
July-Sept 2005	0	4	0	0	0	0	0	0	0	2	6
Re-interviewed Jan-Mar 2006	1	7	0	0	1	0	0	0	3	0	12

<sup>31</sup> I double-counted individuals who had more than one role within the origins and development of UK Biobank. For example a member of the science committee and a spoke member was counted in both categories.

### *Rationale for Sample Composition*

I conducted 76 oral history interviews to gain a representative sample of those involved in origins and development of UK Biobank and to protect interviewees' identities. I wanted to interview a range of interviewees within each group involved in UK Biobank, such as several members of each of the current and previous committees, several members of each of the six spokes, a senior representative of each of the funding bodies, and several representatives of the hub. Given the sensitivities surrounding the origins and development of UK Biobank, interviewing a substantial number of representatives from each group reassured respondents that their identities would be protected and thereby encouraged participation in my research.

I interviewed these groups as their opinions and experiences were the most relevant to my research question of how and why was UK Biobank initially configured in the manner it was? As I was researching the origins and development of UK Biobank, I felt that it was appropriate to interview those formerly involved in the resource as well as those currently involved. I targeted those representing a range of academic backgrounds to minimise the potential for bias involved focussing on one particular sub-group. For the follow-up interviews, I approached a selection of the original interviewees as I felt that it would be beneficial to speak to the same people and gain their reactions to the changes. From a practical point of view, it was also easier to arrange and speak to people familiar with me and my research. I interviewed a representative from each spoke and a representative from each of the main groupings including the hub, the funding bodies and the current committees to gain a balanced view and access a range of perspectives on the changes.

For the main sample, I initially intended to interview equal numbers of individuals directly and indirectly involved in UK Biobank, the latter including academic scientists in the wider scientific community not involved in the resource and science journalists. I felt that interviewing equal numbers in these distinct groups would offer fuller understanding of the issues involved in the origins and development of UK Biobank. It would also partly address the issue of bias that may emerge as a result of just speaking to academic scientists directly involved in UK Biobank. However, I soon realised that this was neither practical nor appropriate. Given the number of



interviews with people directly involved in UK Biobank needed to protect interviewees' identities, there was simply not enough time to interview equal numbers of individuals in each group. I also realised that awareness of the initiative was heavily biased towards those directly involved in UK Biobank. It would have been very difficult to find equivalent numbers of interviewees who were aware of UK Biobank, but were not directly involved in its origins and development. Hence given the nature of my research, it would not have been worthwhile to conduct many interviews with those indirectly involved. I did however interview a small selection of this group to address this issue of bias and gain a fuller understanding. I therefore approached unsuccessful spoke members and senior members of the academic scientific community who were no longer involved or indirectly involved, which meant that they were not formally involved in the initiative yet still had knowledge of it.

### *Sample Selection*

I largely selected interviewees using publicly available information on the UK Biobank website, such as membership of current committees. I selected interviewees on the basis of those representing different professional backgrounds (for example, epidemiology and general practice) and senior figures heavily associated with the origins of UK Biobank. However, as certain information was not publicly available, such as membership of the spokes and some previous committees, I relied to some degree on snowball sampling.

Snowball sampling was successful and interviewees were generally forthcoming when asked who else they thought I should interview. There were however complications. For example, there was one case of mistaken identity. Several interviewees recommended that I interview a member of a previous committee, whom I approached. Unfortunately he shared the same name, worked in the same institution and in the same field as the person I actually contacted, but had recently moved to another university. To complicate matters further the person I contacted did have some previous experience with UK Biobank, the nature of which I still do not know. He demanded to know how I came across his name and on what basis I had selected him. He implied that if the MRC had given me his name, then confidentiality rules may have been breached. It was only after a number of awkward emails that we

realised the mistake and worked out that he had not in fact served on the committee but his namesake had. Snowball sampling elicited further interesting responses, such as an interviewee who recommended an individual whom they thought I should *not* interview. Having had already undertaken this interview the previous week it was clear why this person did not want me to approach this senior figure. These reactions are indicative of the difficulty of conducting research on an evolving and controversial resource. They point to the existing tensions between colleagues working together on an ongoing project and reflect the attempts of interviewees to influence the direction of my research.

The membership of the six spokes was not publicly available information and as requests to the hub for details of spoke membership to the hub were unsuccessful, I had to make a formal enquiry to senior members of each spoke whom I had already interviewed (and whose names were publicly available). This elicited a mixed response. Some gave me the full list of members as requested, others the names of members that they had the permission to pass on, and others the names of those who agreed to an interview. These restrictions were problematic. First of all it meant that I could not easily select my sample on the basis of representing different professional backgrounds. It meant that agreement to the interviews had not been solicited directly through me but via another interviewee. Although they were then contacted by me in the standard way their motivations for taking part were coloured by their relationship with their colleague. Their understanding of the research was often flawed, as it had not been initially mediated through me. In being provided with the names of people who had agreed to an interview, I felt beholden to carry out interviews with all of them, which on one notable occasion led to me interviewing a far larger number of one spoke's members than I had intended.

### 2.3.2 Access

I contacted potential interviewees directly via a letter to their place of work inviting them to take part in my research (see appendix B1). I enclosed an information sheet (see appendix B2) and a consent form (see appendix B3). I considered using gatekeepers rather than approaching interviewees directly but decided that it was inappropriate. Although it may have reassured some interviewees that it was okay to

participate in my research, it was difficult to identify a relevant figure given the structure of UK Biobank and the senior position of the interviewees. Also, I decided that it may actually deter people from taking part; such was the sensitivity of the research I felt that interviewees might not want colleagues to know whether they had participated.

The tone of the invitation letter was formal but friendly. I used MRC headed notepaper to gain a sense of formality, and referred to my supervisors to reassure interviewees that I was conducting bona-fide research. In the invitation letter, I stressed that I was flexible regarding the date, time, location and duration of the interview. I also gave interviewees the option of a half hour telephone interview if they could not afford to meet in person for an hour. I felt that it was important to give interviewees options regarding the practicalities of the interview to increase participation, given their time pressures. In the information sheet, I detailed the aims of my research and the nature of my methods. I detailed the types of people I was contacting and explained why these groups had been chosen. Again, given the schedules of the interviewees, I kept the information sheet concise whilst emphasising the steps I would take to ensure that the interview caused them minimum inconvenience. I stressed that my research was ethically approved and that the interview would be conducted appropriately. I will detail these procedures more fully later in the chapter. When there was no reply to my invitation letter, I resent the letter after one month. If the second invitation letter yielded no response I made no further attempts. Following a positive response, arrangements for the interview were made via email, often through their Personal Assistants.

### 2.3.3 Response

#### *Positive Responses*

Despite the sensitivity of the research and the status of interviewees, the response to requests for an interview was generally positive. For the main study, 69 of the 89 approached for an interview agreed, and 64 interviews took place (see table 1). Interviewees were generally eager to share their experiences and opinions, whatever their stance. There are a number of explanations for the positive response. Some were simply interested in the research and as a result genuinely wished to contribute.

Others had an axe to grind and saw participation as an opportunity to do so, and others saw it as a chance to set the record straight. Interviewees with serious grievances especially welcomed the opportunity to talk about the resource in a confidential manner, and some expressed gratitude at being given the opportunity to do so. Given the numbers approached, the particularly positive response from spoke members (40 of the 43 approached agreed to an interview) perhaps reflects their concerns with the organisational structure, which are addressed throughout the findings chapters. The comparatively low response from those indirectly involved (5 of the 11 approached) in the resource reflects the difficulties I experienced in engaging such individuals in the interview context, which was an unexpected outcome. The response to the follow-up interviews was also positive and all twelve of those approached agreed to the interview. This favourable response may have been because of their familiarity with me and my research, but interviewees were also eager to revisit issues particularly because of the organisational changes.

### *Negative Responses*

The controversy surrounding UK Biobank and the time pressures on interviewees did however affect the response to requests for an interview. Those individuals who declined to be interviewed mostly cited time pressure, although two senior figures who said they were too busy suggested another representative of their particular group. This was however complicated as the alternative peoples' motivations for taking part in the research could have been coloured by their relationship with the individual who put them forward for the interview. Also, one of the alternative people suggested was relatively junior and new to UK Biobank and hence the interview was of limited worth. I also encountered animosity in requesting an interview because of the sensitivity of my research. For example, a current committee member replied to my invitation letter by questioning the merits and motivations for my research and stated that he would actively deter others from participating. Some who agreed, albeit reluctantly, and some who disagreed, reported on how they had contacted MRC Head Office to check that I was legitimate. These responses contributed to a power imbalance in the interviews and were difficult to overcome.

### 2.3.4 Ethics

My research was approved by the University of Glasgow's Faculty of Law, Business and Social Sciences Research Ethics Committee. Staff or students are required to seek such approval if their research involves human participants. I was required to detail the purpose of my research, the methods employed and the procedures adopted.

The ethical considerations for my research concerned the issue of confidentiality. Given the controversy surrounding UK Biobank, and the extent to which interviewees were involved in its origins, and continued to be involved in its development, it was imperative that I took the appropriate steps to ensure the protection of their identities.

### 2.3.5 Confidentiality

The issue of confidentiality was paramount in conducting the oral history interviews. Many respondents were extremely concerned that their identity would not be disclosed and sought reassurance that I would take appropriate measures to prevent this happening. This concern manifested in various ways. For example, one interviewee requested a confidentiality agreement made through legal representation, some requested that the recording be destroyed immediately following transcription and others (6 of the 64) did not agree to the interview being recorded at all (see table 1). I adopted a series of procedures to protect interviewees' identities, which I will discuss. These procedures were however complicated by unforeseen issues, such as the possibility of deductive disclosure and the behaviour of some interviewees, which made the protection of interviewees' identities a significant challenge. I will now discuss the procedures adopted to protect interviewees' identities and the issues faced in implementing them. These procedures are unusual in historical research and most contemporary historians do not conceal interviewees' identities (see 1.3.1 (b) for a discussion of the methodological issues facing the contemporary historian). However, I felt that the controversy surrounding the timing and organisational structure of UK Biobank, exacerbated by its evolving nature, justified my decision to depart from standard historical practice.

### *Confidentiality Procedures*

The procedures I adopted to protect identities largely concerned the appropriate descriptors for interviewees. Each interviewee completed two consent forms. The first consent form (see appendix B3) checked that they were aware of the nature of the research, happy for it to go ahead and sought their permission for the interview to be recorded. This was sent out with the invitation letter and information sheet. The second consent form (see appendix B4) concerned the protection of their identity, whether they wanted to be identified or how their comments were to be anonymised, and if they would like to see a copy of the transcript. This form was discussed at the beginning of the interview and completed at the end, allowing a more informed choice. If they opted for their identity not to be disclosed, I sought their permission to refer to them by the nature of their involvement, for example ‘member of the science committee’, or by using a professional descriptor such as ‘epidemiologist’. If they choose to be sent a copy of the transcript, upon its return I included a letter explaining how I would anonymise it and use the information in it (see appendix B5). I requested that if they wished to make any changes they would have to return it to me within three months. In the returned transcript all identifying information that would need to be changed, such as place of work, was identified with square brackets. This gave interviewees the opportunity to check they were satisfied with the level of anonymisation, correct any errors and make any clarifications. These procedures alone proved to be insufficient to protect every interviewee’s identity and had to be adjusted in response to a number of issues.

The exceptionally large number of interviews carried out, particularly with multiple members of each committee, meant that reference to nature of involvement (for example, ‘member of the science committee’) was generally an acceptable measure and did not identify people. However, there were limitations to the extent that involvement could be described. For example, it was inappropriate to refer to positions within committees such as chair, spoke lead or co-ordinator. It was inappropriate to distinguish between the spokes (for example, member of the Scottish spoke), as deductive disclosure could reveal the identity of respondents. Also, this procedure was not acceptable for every interviewee and the nature of the response had implications on the extent to which involvement could be described. For example, one respondent, involved at a senior level, was particularly candid and as such it was not

appropriate to describe his involvement in UK Biobank as it could identify him. He indicated during the interview the parts of the recording which he did not wish to be attributed to his involvement and suggested an alternative descriptor that referred to his professional position.

As only a small proportion of my sample were women (14 of the 64 interviewees), reference to an interviewee as a woman made her potentially identifiable. This was exacerbated by the distribution of females in the organisational structure. For example there was only one woman on the EWG and three on the PDC. I therefore decided to adopt the generic 'he' pronoun throughout the thesis to refer to men and women. I considered randomly assigning 'he' or 'she' or gendered pronouns to quotations but felt that even with explanation to the contrary the reader may have assumed the usage to be correct. This decision was contrary to British Sociological Association (BSA) Equality and Diversity Sex and Gender Guidelines (2004) that advise against the use of the generic 'he' but I argue that it is justified in this particular case given the likelihood that respondents' gender could render an interviewee identifiable. It was therefore an empirical decision adopted to protect interviewees' identities, which was supported by the fact that gender did not emerge as a factor in my research (see 2.3.9).

I included the professional descriptor (for example, 'epidemiologist') as well as the description of the nature of involvement in UK Biobank to enable comment on any pattern from the responses of different professional backgrounds. This procedure was, however, complicated as if I wanted to comment on responses common to a professional background within a group it could have identified respondents. For example, there was only one representative from general practice on one of the committees. In order for me to use specific professional descriptors the group had to be sufficiently large and varied, such as a pattern in the responses given by GP spoke members. On occasion, it was not appropriate at all to refer to professional background, either in the context of the sample as a whole or within a group. For example, there were only two lawyers involved, one on the IAG and the other on the EGC. Interviewees often required reassurance on the matter of professional descriptors and I had to make clear that I would only refer to their professional descriptor in a way that would not identify them. In retrospect, as patterns did not emerge according to profession this issue did not materialise in writing-up.

*Issues that complicated confidentiality procedures*

These procedures to protect identities were further complicated by unforeseen issues, for example potential deductive disclosure and the behaviour of interviewees. In some cases the procedures were altered as a result of these issues, whereas in other cases these issues caused me to adapt my personal approach to the interviewees.

Potential deductive disclosure was a serious issue in ensuring the protection of people's identity. The large number of interviewees addressed this problem effectively in most cases but identification procedures had to be modified with it in mind. For example, the number of respondents, albeit small, who opted to be identified proved an issue. It became clear that by identifying them, the process of deductive disclosure could reveal the identity of others who did not wish to be identified. I decided that it was inappropriate to identify anyone at all. Deductive disclosure was also an issue when the identity of an interviewee was strongly implied in their response, for example if they had a particular viewpoint or experience well known in their professional community. In these circumstances there was a certain inevitability regarding the disclosure of identity if the responses were used in the intended manner. Some interviewees to whom this applied conceded this inevitability and were happy for the implication to be made. Others requested that all such information which implicated them in this manner not be used at all. This often meant that key information was lost and I had to handle their transcript extremely carefully and not use it to its full potential. As a hypothetical example, suppose one respondent was a key figure in the discussions of the potential for UK Biobank to address cardiovascular disease. The mere mention of cardiovascular disease in connection with his involvement would have revealed his identity; therefore none of this information could be used. Others requested special measures that allowed me to use the information but only by prior consultation with them. In these circumstances, I agreed that if I heavily referred to their transcript in a particular section, I would send them a draft of that section to ensure they were comfortable with it. Certain interviewees requested this as a condition of their participation, given the likelihood that the comments would identify them. Fortunately, few requested this measure as it would have been difficult to implement on a large scale. However, given that I generally did not refer heavily on any single interview throughout an entire section



this did not prove to be too much of a concern and this only applied to one interviewee.

The behaviour of certain interviewees complicated the procedures adopted to protect respondents' identities, specifically the procedures concerning transcript return. The decision to offer interviewees the opportunity to see a copy of the transcript was advantageous in allaying fears and encouraging participation but it was a complicated procedure to implement. Practically, there was a potential for delay in responding to any concerns that interviewees had with the transcript and in the process of checking and returning transcripts promptly. A further issue was the danger that interviewees would substantially alter the content of the transcript, limiting the value of the interview. This issue was particularly worrying regarding the more controversial interviews. As much of the concern surrounding the use of the transcript came from misconceptions regarding qualitative research, I included in the letter accompanying the transcript an explanation of how I would use any quotations (see appendix B5). For example, some believed that their interview would form the basis of a whole chapter and would be presented in its entirety. I stressed in the letter how their comments would not be used in isolation and would be illustrative of general themes.

Overall, however, the process of transcript return proved successful. A large minority, 26 of the 64 interviewees in the main study, did not opt to see a copy of the transcript (see table 3). The response to this offer was highly polarised, with some making it clear that in no circumstance would they like to see the transcript and others eager to get a copy as soon as possible. As far as any pattern was discernible, generally senior respondents did not wish to see a copy while junior respondents were far keener to see the transcript, with some notable exceptions. The majority of interviewees in the follow-up study did opt to see a copy of the transcript (9 of the 12), several of whom had not requested to see it in the main study. This may reflect the caution felt by some interviewees who took part in the follow-up study as a result of the sensitivities surrounding the organisational changes. The process of transcript return had unforeseen advantages in keeping the channels of communication open with interviewees, and obtaining useful information regarding the development of UK Biobank before it was made public. Interviewees who requested a copy of the transcript returned it promptly and with minor changes. Surprisingly, these changes

largely concerned grammatical issues, such as one respondent who requested that all ‘it’s’ be replaced with ‘it is’ and another that all ‘I means’ be removed. This in itself was interesting: the importance that some scientists placed upon removing colloquialisms betrayed misunderstandings about the purpose of the transcripts. It was as if they viewed their transcripts as akin to an official press release, and wished to retain an air of professionalism within their written opinions.

Table 3: Transcript Return

	Hub	Spoke	Science Comm.	EGC	BoD	IAG	PDC	EWG	Funders	Indirectly Involved	Male	Female	Total
No. requested transcript	4	24	4	2	4	2	5	2	3	1	27	11	38
No. re-interviewed requested transcript	1	6	-	-	0	-	-	-	2	-	6	3	9

There was however a notable exception to the reaction of interviewees to the transcript; one interviewee made substantial changes to the content of the interview. He deleted several passages and replaced them with alternative responses, explaining that following the changes to the organisational structure these alterations made the transcript more relevant. The interview took place in the last stage of my initial period of fieldwork prior to the changes, but the transcript was returned to me after the changes. His alterations to the transcript revealed misunderstandings regarding the nature of my research. He believed that I was trying to produce a factual, strictly narrative account of proceedings and was not interested in reporting issues that complicated the development of UK Biobank. Hence he adapted his responses to represent a coherent process devoid of complication. His alterations also revealed uneasiness with the content of the transcript in general. It was a particularly frank interview and perhaps he regretted making such comments, especially after being confronted with them on paper in their entirety. Following further explanation of the nature of my research and reassurance regarding the procedures implemented to protect his identity he consented to use of the original transcript. These explanations and reassurances were not made directly from myself but were rather mediated

through my supervisors. We agreed that, given the seriousness of the issue and the concern of the interviewee, he may be more comfortable with the assurances of a senior researcher.

The behaviour of certain interviewees also complicated the procedures adopted in a general sense. For example, certain interviewees, often senior, asked me who else I had interviewed and what they had said. They did so subtly, on and off tape, commonly at the beginning or the end of the interview when my guard was down. I found these requests surprisingly difficult to cope with when they came from senior figures in their homes or offices, given the power relations. The questions included direct requests such as 'did you speak to X' and indirect questions such as 'I bet X had some interesting responses' or 'what did X say' or 'I heard you spoke to X, what did they say'. I was very careful not to be caught out as I could not reveal who I had interviewed and I especially could not detail their responses. Early on I realised the importance of developing a standard response to such queries, by politely but firmly stating that I could not reveal individual identities or responses but instead I could refer to the types of people I was approaching and that everyone was asked similar questions. Interviewees seemed to be unsure if there was an official line they should be following, reflecting the uncertainty regarding the development of UK Biobank and the lack of a recognised version of events for them to refer to.

### 2.3.6 Pilot Interviews

I conducted two pilot interviews in order to become familiar with the issues involved in interviewing elites on the origins and development of UK Biobank. I interviewed an academic scientist who was a member of a previous committee and a representative of the funding bodies. The academic scientist interviewed in the pilot study later agreed to take part in the main study.

These interviews were useful and I gained worthwhile experience of interviewing elites on controversial issues. I also gained practical experience of interviewing in unfamiliar locations and environments and of using the appropriate equipment to record interviews. The pilot interviews gave me greater awareness of the complexities of ensuring confidentiality, as well as the opportunity to gauge the appropriateness of

the ethical procedures implemented to protect interviewees' identities. I also assessed the usefulness of the interview schedule, which changed considerably following the pilot interviews. The questions became more focussed and were arranged into distinct phases in the development of UK Biobank. Following the pilot interviews, I amended the wording of some questions to avoid the misinterpretations that I encountered in conducting the pilot interviews.

Given the sensitivity of the research, I was reluctant to carry out more pilot interviews as I felt that it would have been inappropriate. Also, I did not want jeopardise involvement in the main study by conducting extensive pilot interviews with people under significant time pressures, who may be unable to participate in more than one interview.

### 2.3.7 Schedule

I did not vary the interview schedule significantly between interviewees and only altered it depending on their personal experience (see appendix B6). For example, an interview with a member of the PDC focussed on their experience of that Committee. I organised the schedule chronologically into phases in the development of UK Biobank (such as the origins of the idea, protocol development and organisational structure) and separated it into particular issues (such as role of the funding bodies). I did not alter the order of the questions and I asked every interviewee about the same topics. I began a particular section with a general question, avoided leading questions, and used follow-up questions accordingly. These follow-up questions would be more specific in nature and I rarely had to refer to them as respondents were generally very open. This semi-structured approach allowed me to divert attention from the schedule, and investigate particularly interesting, unusual or strongly expressed responses. I followed the same principles in designing the interview schedule for the follow-up interviews (see appendix B7), but the questions themselves only concerned the organisational changes. I limited the number of questions asked as I assured interviewees that the interview would not last longer than half an hour. However, as I was familiar with respondents and they were familiar with me and my research there was less need for explanation and by focussing solely on the changes these follow-up interviews did not tend to overrun.

The response to the schedule was generally positive and only a few interviewees replied 'no comment' to questions. Some interviewees requested that the tape be turned off during parts of the interview as they responded to particular questions or elaborated on specific issues. Some allowed me to take notes on these comments, whereas others requested that I did not record them in any way and made them off the record. Similarly, at the end of the interview, once the tape was switched off some interviewees made extensive comments and elaborated on their responses, meaning I could not use any of the information.

Two respondents requested to see the interview schedule in advance, which I allowed. I did not offer this procedure but felt obliged to carry out their request given their agreement to the interview. I was however anxious about doing so and worried that it would yield formulaic or rehearsed responses to the questions. In reality I feel that it made no difference to the nature of the interview; one of the interviewees admitted to having lost the schedule, and the other confessed that he had not looked at it until the time of the interview.

#### 2.3.8 Telephone Interviews

I conducted the majority of interviews in the main study face to face (42 of the 64) and only 22 of the 64 were conducted over the telephone. However, I conducted the vast majority of the follow-up interviews over the telephone (11 of the 12). For the main phase of fieldwork, I offered interviewees the choice of a face to face interview lasting about an hour, or a telephone interview lasting about half an hour. I gave interviewees the choice primarily to encourage participation given the time pressures faced by interviewees, but stated on the invitation letter that I would prefer to conduct the interview in person. I conducted the follow-up interviews over the telephone due to my time and budget constraints. I undertook these interviews beyond my official period of fieldwork and hence I could not afford any further travel time and cost. One follow-up interview was conducted face to face as at the time I was sufficiently close to the individual and it was therefore more practical.

There were advantages and disadvantages to conducting telephone interviews in the main phase of fieldwork. I believe that offering telephone interviews increased participation in my research as interviewees had very busy schedules. Telephone interviews also allowed me to interview people who lived outside the UK whom it would not have been possible to speak to otherwise. It was however difficult to establish a rapport with the interviewee, which was exacerbated by the relatively short length of the interview. Some interviewees were distracted throughout the interview and it was clear that other tasks were being undertaken, such as typing. Establishing rapport was further complicated over the telephone as I had to complete the consent forms on their behalf, which meant carefully reading them out verbatim. I also encountered practical difficulties in conducting telephone interviews. For example, when the interviewee did not wish the interview to be recorded, it was difficult to hold the receiver in one hand and take detailed notes in the other. Despite interviewees opting for the telephone interview option because of their time pressures, many lasted well beyond the half hour allocation. It may have been the case that some interviewees just preferred the telephone option regardless of time pressures.

### 2.3.9 Researching Elites

The issue of power dynamics was relevant to my research in that I, a young, female student, conducted oral history interviewees with some of the most senior scientists in the country. The interviewees were predominantly male, middle-aged medical scientists, and included senior figures within the MRC, Wellcome Trust, DoH and the Scottish Executive. The fact that I occupied the position of an outsider on account of these differences also influenced my research. The following issues affected the power dynamics of the oral history interviews: age, gender, academic background, location and arrangements of the interviews, and the evolving nature of UK Biobank. I will consider the effect of each of these issues on the interview interaction, detail the steps I took to address the power balance, and evaluate the advantages and disadvantages of the power dynamics and my status as an outsider.

#### *Age*

I felt that my age had a considerable effect on the power dynamics of the interview. There was less of a power imbalance in interviews with younger participants. In the

few interviews with individuals of a similar age there was a greater sense of equality and they were more able to relate to my PhD student status. It is difficult to draw any conclusions from this experience as these interviewees held relatively junior positions within UK Biobank, and all came from the same spoke group. They were fairly new to UK Biobank and hence less familiar with its origins and development, and one was suggested as an alternative by the more senior individual originally approached. It is therefore difficult to say whether their age or lack of experience, and therefore stake in the initiative, contributed to the erosion of the power imbalance. The power imbalance between me and interviewees was reinforced in interviews with older participants. Some older interviewees remarked upon my age and seemed to take me and my research less seriously. Although their attitude was very friendly and contributed to the feeling of rapport, it allowed interviewees to control the interview. It was as if they viewed me as akin to a daughter and would cheerfully discuss how their own children were faring at university whilst carefully avoiding the questions.

### *Gender*

Gender may have further affected the power balance of the interviews, and the vast majority of interviewees were male (50 of the 64 main study interviewees, 9 of the 12 follow-up study interviewees). Interviews with women were generally more informal and there seemed to be less of a power imbalance. However, it is difficult to draw any conclusions regarding the effect of gender on the power dynamics of the interviews as age was a significant contributory factor in these cases. For example, the power imbalance was more pronounced with older female interviewees and less obvious with younger female interviewees.

### *Academic Background*

My academic background, specifically as a social scientist, historian, qualitative researcher and MRC funded student contributed to the power imbalance in the oral history interviews.

The convergence of different academic backgrounds between me as a social scientist and interviewees as scientists caused misconceptions regarding the nature of my research. These misconceptions contributed to the power imbalance of the interview as they sometimes resulted in a certain animosity toward me and my research. For

example, some scientists conceived of my PhD as a scientific evaluation of UK Biobank aiming to prove or disprove its worth, as opposed to analysing the issues surrounding its origins and development. These interviewees therefore questioned my ability, or lack of, to conduct an evaluation and expressed confusion at the types of questions I was asking. Other interviewees would laboriously try to explain complicated scientific theory, which coupled with the animosity and confusion, reinforced the power imbalance.

Similarly, my role as a contemporary historian and qualitative researcher reinforced the power imbalance, on account of different understandings of contemporary history and qualitative research. Some interviewees understood historical research as the construction of a chronology of events, of forming a strictly narrative account of proceedings. Given their perception that I was trying to gather reliable, factual data, they questioned the validity of conducting oral history interviews and were surprised at the types of questions I was asking. They were preoccupied with the specific dates of meetings and some interviewees even prepared such information in advance. The effect of such understandings on the power imbalance was exacerbated by interviewees doubting the merits of UK Biobank as qualifying for historical analysis at all, with many staunchly of the belief that it did not. Some interviewees took issue with the contemporary historical nature of my research and remarked on how UK Biobank itself had not formally begun to recruit participants. I found these opinions challenging, especially as they were expressed so vociferously by senior individuals, and they served to reinforce their authority in the interview.

Interviewees' understandings of qualitative research led to criticism of my research, specifically my choice of methods, which further served to reinforce the power imbalance. Some interviewees doubted the worth of oral history interviews, of seeking opinions and personal experiences. They questioned the reliability of memory and felt that asking for recollections was flawed. Interviewees became frustrated as they struggled to recall a particular date when a meeting occurred or as they described their feelings on a particular issue, believing that I was basing my research on factual, chronological information. These understandings and consequent criticisms were difficult to overcome, especially in the context of an interview and thereby largely contributed to the power imbalance.



Another facet of my academic background that led to hostility and therefore affected the power balance in the interview was that I was an MRC funded student researching an initiative partly funded by the MRC. Some interviewees regarded me as a secret investigator for the MRC reporting back their responses to the funding bodies, which reflected the difficult relationship between some academic scientists and the funding bodies. Others believed I was compiling a press release for the MRC, strongly endorsing UK Biobank. They therefore questioned the funding for my PhD, the relationship between MRC Head Office and my host Unit, and sought reassurance that I was not acting on behalf of the MRC. A further powerful misconception was that I was undertaking the role of a journalist trying to condemn UK Biobank in a tabloid-like style. I was therefore perceived as having a strong agenda to pursue with the sole motivation to expose UK Biobank negatively, for example as a waste of public money. These perceptions heightened my sense of powerlessness as I struggled to overcome them and explain my position.

#### *Location and Length of Oral History Interviews*

The procedures I adopted in arranging the oral history interviews contributed to the power imbalance in that control over the time, place and location of the interview lay entirely with interviewees. This meant that interviews took place in locations and offices entirely unfamiliar to me throughout the UK. Interviews took place in hospitals, university buildings and funding body headquarters in private offices and one interview was conducted in an interviewee's home. Having been in a university environment for the past few years, I was less anxious about meeting in university buildings despite their unfamiliar location. It was however quite daunting meeting in hospitals, laboratories and funding bodies' headquarters due to their unfamiliarity, and also because they highlighted the difference in academic background between me, as a historian and social scientist, and the interviewees largely with medical science backgrounds.

Interviewees also controlled the time and length of the interview. I requested that interviews lasting about an hour in person and offered shorter telephone interviews lasting half an hour. Some interviewees, having agreed to an interview in person, would stress at the start of the interview that they could not afford to give me that

much time and would not then specify an appropriate length. This contributed to a feeling of powerlessness on my part as I would attempt to amend the interview schedule without knowing what time was actually available. Despite such assertions, these interviews would last about an hour and often longer. Nevertheless, I had to be prepared to amend the interview schedule in response to changing circumstances. For example, on one occasion an interviewee was forty minutes late and then could only give me ten minutes. These uncertainties contributed to the power imbalance between me and interviewees.

### *Evolving Nature of UK Biobank*

The evolving nature of UK Biobank meant that my role and research were under particular scrutiny, which contributed to the power imbalance. When I began this PhD in October 2003 UK Biobank was supposed to have already started, with recruitment of participants planned for earlier that year. The ongoing scientific and organisational uncertainty strongly affected respondents' reaction to and perception of my research, which in turn affected the interview context. For example, the response to questions about the organisational model was indicative of the uncertain situation, with some respondents considering what they *should* say. It was as though some interviewees were struggling to articulate a party line or universal message approved from the centre, complicated by the fact that the centre was not occupying a decisive leadership role. Similarly, respondents would ask what others had said, including respondents within particular groups asking what their colleagues had opted for on the second consent form. As a result of UK Biobank's evolving nature, some interviewees were very suspicious of my motives. For example, all of the interviewees within a particular group asked me what I hoped to achieve in writing a thesis on this subject, aside from obtaining a PhD. It was challenging to assert myself in these circumstances, given the seniority of the interviewees.

### *Advantages and Disadvantages of Power Imbalance and Outsider Status*

Despite the difficulties caused by the balance of power in the interviews, at times it was beneficial. For example, given my age, gender and academic background I was not perceived as a threat. This non-threatening status was advantageous on account of the controversy surrounding UK Biobank. Some interviewees were encouraged by it and were more open on account. In the same way I felt that my academic background

in particular set me apart as an outsider. Interviewees did not make assumptions regarding my knowledge of UK Biobank and the fact that I was an outsider encouraged an openness that may have been difficult had I been at all involved in the field.

Although interviewees' control over the time, location and duration of the interviews contributed to the power imbalance, it reassured interviewees that I was sensitive to their commitments and would endeavour to cause them minimal disturbance, which encouraged participation. Also, discussion of my travel arrangements and impression of the locations and building served as a useful ice-breaker and relieved tension. My MRC funded status was also advantageous and, whilst it was a source of tension with some interviewees, it put others at ease to know that it was a legitimate research activity. In this way, I believe that it offered reassurance to some interviewees who otherwise might not have agreed to the interview.

I took a number of steps to address the power imbalance in the interviews and tried to minimise its effect. For example, I addressed the difference in professional status by dressing smartly, thereby asserting myself as a researcher rather than a student. To lessen the effects of conducting the interview in an unfamiliar location and building, I arrived early and familiarised myself fully with the building and location of the office. In taking such steps I avoided getting lost, arriving late and being flustered. My confidence and abilities grew as the period of fieldwork went on, which also addressed the power imbalance. I feel that the significance of power balance was lessened due to the formal topic and the professional status of the interviewees. They were familiar with the interview process albeit in different settings, such as being interviewed for the media or conducting interviews themselves as part of a research project.

I addressed the power imbalance arising from misunderstandings of my research with full and frank discussion of the nature of my research, which lessened animosity and confusion and led to a more open interview. I carefully explained what I was not trying to do as well as exactly what I was trying to do. Regarding the effect of different understandings of contemporary history and criticism of the timing of my research, I explained why I was conducting a contemporary history at that stage and

that I was researching its origins and development. I also detailed the advantages of embarking on such a study and interviewing the key players at that particular stage.

## 2.4 Archival Research

### 2.4.1 Access

I applied to both the MRC and Wellcome Trust for access to official documents concerning the origins and development of UK Biobank. As the two main funding bodies, I felt that it was important to analyse both funding bodies' sets of documents to gain a fuller understanding and to compare their involvement in UK Biobank. I considered applying to access the documents at the DoH but felt that there was not enough time.

The initial request for access was made via my supervisors, through contacts in the MRC and the Wellcome Trust. We felt that, given the status and nature of the documents, it would be more appropriate and successful than a direct request from me. I was granted access to the MRC, but denied access to the Wellcome Trust. The Wellcome Trust argued that as the documents were still in use I should not be allowed access. The documents were also still in use at the MRC but this did not hinder access. The fact that I am an MRC funded student may have accounted for being granted access to their documents. Given the controversy surrounding UK Biobank, the decision of the Wellcome Trust and the live status of the documents, I was surprised at the level of access given to the MRC documents. The 'live' status meant the MRC were under no obligation to provide any access, although as they are a public body I may have been able to argue terms through the Freedom of Information (FOI) Act 2000 that came into full force in January 2005. Interestingly, requests by others to see the anonymous comments of the peer reviewers made under this Act were successful and as a result of this they were placed on the MRC website in May 2005.

#### *Nature of the Documents*

The types of documents analysed at the MRC varied widely in nature and detail. They included official minutes of meetings of previous committees significant in the development of UK Biobank, such as the EWG and the PDC. These were important documents with considerable detail and some even attached identities to each of the members' comments. Emails were a prolific and useful source given the clarity of

information such as sender, receivers, date and subject information. There were emails between committee members, representatives of the funding bodies and committee members, senior representatives of the funding bodies and MRC colleagues. Official correspondence included letters of instruction to the peer reviewers and notification including feedback to unsuccessful hub and spoke bidders.

### *Coverage of the Documents*

Although the extent of coverage varied, each of the key stages in the development of UK Biobank was documented in this material, such as the peer review process, the funding decision, and the hub and spoke bidding process. Highly controversial episodes were also documented, such as contract negotiation and protocol development. Archival analysis was particularly useful for building up an accurate chronology of events, which was not possible through oral history interviews. These documents were an invaluable source in understanding the key events in the origins of UK Biobank, the issues behind them and the central players involved. Archival analysis therefore complemented understanding of the themes that emerged from the oral history interviews. The information accessed was not available elsewhere, especially regarding the role of the early committees. The documents therefore offered different insights into the origins and development of UK Biobank.

The coverage spanned from 1998 until 2004, reflecting the increasing role of the hub and the diminishing role of the MRC, in taking UK Biobank forward. The last key episode documented was initial contract negotiation between the hub and the spokes. There were approximately one hundred volumes of files, which I spent about two months in London analysing. There were however gaps in the coverage and it was clear that not every episode was documented. For example, there were no minutes of current committee meetings, such as the Science Committee. This may be as a result of the timing as the documents largely concerned the origins and development of UK Biobank and did not really continue once the hub was established, except for the process of contract negotiation. Also, there was also no documentation in the material I analysed of any debate regarding the selection of the hub and spoke model, which is unfortunate as it was a significant issue.

## 2.4.2 Confidentiality

The status of the documents meant that my access was not monitored by a trained archivist but by a member of MRC Corporate Affairs who was not fully aware of the content of the files, which led to difficulties. The initial procedure agreed was that I would signal any documents that I was interested in and the representative from Corporate Affairs would photocopy them. However they were daunted by the number and type of documents I wanted copied. This lack of understanding of my objectives and consequent unease regarding my interest was a particularly difficult issue given the special permission I had to access the material, and the lack of obligation on their part to let me see it. It was clear that they did not want such documents to leave the building and were slightly uncomfortable with me accessing them at all. In response to these concerns, I provided an information sheet and conduct agreement detailing the nature of my research, stating that anonymous material would remain so, agreeing not to photocopy anything, and keeping the same hours as the person monitoring my access (see appendix B8). This strategy led to a number of practical difficulties, such as finding desk space in the busy corporate affairs office leading to protracted visits over a number of months. Despite such difficulties this was necessary and averted the threat of access being jeopardised.

### *Sensitive Information*

A recurring issue in analysing the private documents was the difficulty of handling sensitive information. The nature of this information meant that I could not use it, which was a limitation of the method. For example, there was a substantial amount of material, especially in email form, which documented personal conflicts between key figures in the development of UK Biobank. Similarly, as the documents had not been archived there was much duplicate filing, which although cumbersome allowed me to access several versions of documents, some of which included personal comments pencilled in the margins that were illuminating. Although it would be inappropriate and of limited value to air such private feuds, it was useful in gaining understanding of the tensions that surrounded the development of UK Biobank. Caution also had to be exerted in utilising practical information in the files, such as spoke membership. The full membership of the six spokes, including names and addresses, was available in the documents. However, given that such information was not publicly available

and the sensitivities I encountered in approaching some interviewees (many questioned how I obtained their name even when it was publicly available) it would have been inappropriate to contact individuals this way. This was a difficult decision as it would have saved a lot of time and allowed a more representative sample of spoke members to be selected.

#### 2.4.3 Approach to the Documents

I catalogued every document in terms of subject, personnel and date. The depth of detail taken depended on the significance of the material, and often documents were recorded verbatim. For example, the minutes of the EWG and the PDC were more relevant and demanded a greater level of attention than legal information surrounding the set up of UK Biobank Limited, and the health and safety information in the hub and spoke bids. Given the ongoing development of UK Biobank, I assumed that everything relating to key events was significant; especially as accessing the material in the current form again would be difficult and it was not clear what would and would not continue to change. I was still in the process of defining the focus of my research when I visited MRC headquarters from November 2004 to July 2005. For example, I was aware of the controversy surrounding the hub and spoke model so I assumed everything pertaining to it was significant and paid particular attention to these documents, which is useful given the changes made to the model in 2005.

#### *Issues surrounding the timing of archival research in relation to oral history interviews*

A further issue in my research was the timing of archival research in relation to the conduct of oral history interviews. Analysis of the material relating to the development of UK Biobank was useful in informing my interview schedule. The opportunity to do this however depended on when information was gathered from the documents and when interviews with those involved took place. The extent to which analysis of the documents could inform the topic guide had to be carefully handled, to avoid asking leading questions.

I found interviewing respondents on the same issues that had been recently analysed in the documents difficult at times. I had to react appropriately. For example, I could



not show any surprise when a response contradicted what was recorded in the files, or any acknowledgement when their accounts would correlate closely with the information in the documents. For example, one senior respondent detailed a very different reaction to a controversial element of protocol development in the interview than was stated in the files. On the other hand, when a member of the PDC referred to a letter he had written to the group's chairman expressing concerns about the committee, his account of it corroborated almost exactly with the letter contained in the documents. It was important that I examined discrepancies between what was recorded in the documents and what was reported in the interviews to gain an understanding of the meanings attached to different sentiments. Following examination, these contrary responses reflected the significance of present identities and events in recollections of previous episodes. For example, one interviewee reported in an interview that he did not support the proposals for a hub and spoke model yet his support for the same model is recorded in the minutes of a previous committee. Given the controversy surrounding the hub and spoke model and its ultimate demise, it is perhaps unsurprising that a senior figure would seek to disassociate himself from its origins.

### *Limitations of Archival Research*

It is important to bear in mind the limitations of archival research. For example, it should be remembered that the files I accessed were not representative of all of the documents pertaining to the origins and development of UK Biobank, and the existing collection was made up of files judged worthy of retaining. The files were preserved because someone decided that they should be kept and it is important to appreciate the significance of decisions to retain some records and discard others. Similarly, it is important to acknowledge the involvement and influence of certain individuals in the content of the records. For example, the content of the minutes of a meeting are at the discretion of the note-taker, which is reflected in the variation regarding the detail of the minutes of various meetings. Furthermore, it was often clear that the documents were not complete; for example, an agenda for a meeting existed but no minutes. The fact that I only accessed the documents pertaining to the origins and development of UK Biobank from the perspective of the MRC was a further limitation of the method. Although some of the material concerned relations with other funding bodies, I was still viewing a one-sided perspective. For example, certain key meetings involving

representatives from all of the funding bodies took place at the Wellcome Trust, and the minutes of those meetings would be held there. Similarly, the role of the Wellcome Trust or the DoH in the origins and development of UK Biobank could not be accessed.

## 2.5 Analysis

### 2.5.1 Thematic Approach

I adopted a broad thematic approach to analysis of the interview material and archival research. Using coloured pens, I coded the transcripts and notes from the archival research into the themes pertaining to the main stages and key issues in the origins and development of UK Biobank. These themes were: origins (EWG), protocol development (PDC and Science Committee), organisational structure (hub and spoke model), role of the funding bodies, consultation, design, motivations for involvement, and development of the EGF (IAG and EGC). I then grouped material from each of these themes into three broad areas that formed the topics of the three findings chapters, which were: the establishment of UK Biobank as a departure from standard academic scientific practice, confusion over control of UK Biobank, and lack of trust between academic scientists, representatives of the funding bodies and UK Biobank Limited.

I adopted a broad thematic approach to my analysis as it was the most appropriate to my research aims and to the data gathered. As I was researching the origins and development of UK Biobank my enquiries focussed on key stages and issues in the development of the resource, which lent itself well to a broad thematic approach. Similarly, the data collected concerned the same stages and issues in the origins and development of UK Biobank; hence it was easily grouped into broad themes.

I began early stages of analysis long before the process of coding the data, which meant that I was already familiar with the data and the potential themes before I began to code. For example, I made extensive field notes immediately following every interview in which I recorded my impressions of the interview and interviewee and the themes that emerged. I listened to the recordings on my return journeys if time and circumstances allowed. Every recorded interview was transcribed by a professional transcription company, Smallbiz Transcripts, who were bound by MRC 'Good Research Practice' guidelines on confidentiality. Following transcription, I read through every transcript carefully to check for spelling errors. I also tried to check every transcript with the recording but the sheer number of transcripts and time

consuming nature of the task complicated this process. I decided to check every transcript with the recording when the transcript was being returned to the interviewee, was particularly significant, or from an underrepresented group. In adopting these criteria I checked the majority of transcripts from the main study [44 of the 64] and all of the transcripts from the follow-up interviews with the recording. Also, if I heavily referred to a transcript or quoted from a transcript that had not been checked against the recording, I would go back and check those passages or quotations in the transcript against the recording.

### 2.5.2 Summaries

Once I coded the interview transcripts and took notes from archival research, I summarised each interview and the findings from archival research.

Each interview summary began with an introduction that included my impressions of the interview and interviewee, any interesting information that did not fit into the designated themes (such as comments regarding my research or terminology), and a list of the themes that emerged. I then devoted a paragraph to each theme. I ended the summary with a very brief conclusion describing the strengths and weaknesses of the interview. I included many quotations in the summaries to fully illustrate the issues of the interview as voiced by interviewees. These summaries were detailed and the majority continued into four or five pages. I considered using computer assisted analysis packages, such as NVIVO, in managing my interview data in particular, but concluded that it was unnecessary in my research. The extensive number of transcripts (76), some in excess of twenty pages meant that it would have been a very labour intensive and time consuming process. Furthermore, given the nature of the data and my broad thematic approach to analysis, I felt that a computer assisted analysis package would not have been helpful. For example, as the same broad themes emerged in each interview it was not difficult to identify them in the transcripts.

I produced a detailed summary of my findings from archival research of the MRC's official documents relating to the origins and development of UK Biobank. I adopted a similar approach in summarising my archival research findings to that of the

interview summaries and presented the data according to the aforementioned themes. I detailed the title, date, people involved and reference number of each document. Again, I included as many quotations as possible in summarising archival research, thereby maintaining a close link with the original material. Although summarising such varied and lengthy material was a challenge, my focus narrowed and my understanding of the issues increased sufficiently to make it a less daunting task. One year had passed from the point that I began to collect the material and summarise it, therefore I found much of the material not relevant to my research. Also, the sensitive nature of much of the material meant that I could not use it, which also lessened the process of summarising.

I produced summaries of the oral history interviews and of the findings from archival research to familiarise myself further with the data and to manage it effectively. The process of summarising and initial data collection was transparent, for example a quotation from an interview or document was referenced with the page number of the transcript as well as the page number of the summary. Compiling summaries of oral history interviews was particularly useful considering the number and length of transcripts. It was much easier to refer to a summary of an interview in the first instance, rather than to an extensive transcript. It also considerably aided analysis, and I found it effective in familiarising myself with the data from every interview. Similarly, the summary of the findings from archival research was far more manageable than sifting through an abundance of material most of which was not relevant. It also gave me the opportunity to reacquaint myself fully with the archival research prior to writing-up, which was important given the time that had passed between archival research and writing. Summarising archival research findings was especially important in my research as the material itself was not archived or presented in any particular order.

The thematic approach adopted toward analysis lent itself well to summarising oral history interviews and archival research and the data closely correlated with the themes. I will now present the findings that emerged from this analysis of interview and archival research data. As discussed, I grouped data from each of the themes pertaining to the main stages and key issues in the origins and development of UK Biobank into three overarching broad areas. These areas formed the topics of the

following three findings chapters: the establishment of UK Biobank as a departure from standard academic scientific practice (chapter four), confusion over control of UK Biobank (chapter five), and lack of trust between academic scientists, representatives of the funding bodies and UK Biobank Limited (chapter six).

## **Chapter 3**

### **Chronology**

#### **3.1 Introduction**

I now provide a detailed chronology of the origins and development of UK Biobank. I have separated the information into six key stages: the development of the proposal for UK Biobank (1998-2000), protocol development and consultation (2001-2003), the funding decision (2002), internal organisation in the funding bodies (2000-2003), implementation of the organisational structure (2003-2005) and organisational changes (2004-2005).<sup>32</sup> Although I have presented this information in chronological order, many of the stages overlap. I also constructed a timeline based on this chronology to assist the reader (see appendix A1) as well as diagram 1 (below).

This chronology is largely based on information gathered from archival research on the MRC documents on UK Biobank (see chapter three for discussion of archival research). These documents spanned the origins of UK Biobank within the MRC in 1998 to the establishment of UK Biobank Limited in December 2003. As the documents did not cover implementation of the organisational structure, this information was gathered from the UK Biobank website as it developed from 2003-2005.<sup>33</sup> I researched UK Biobank from its inception in 1998 until the organisational changes in August 2005, this chronology will therefore cease at August 2005. I also applied to the Wellcome Trust to undertake archival analysis of their documents but as the documents were still in use I was not granted access.

Where possible, I include the names of individuals and groups that were involved in the origins and development of UK Biobank, including former committee members and those that attended key meetings. Rather than provide biographical information on every individual identified in this chronology, I describe the extent of their involvement, if any, in the origins and development of UK Biobank. I have however

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<sup>32</sup> See Appendix A3 for an organisational representation of this chronology

<sup>33</sup> The UK Biobank website underwent significant alteration in style and content during the period of my research (see chapter 7 for more information).

included biographies from the UK Biobank website of those committee members formally involved in the initiative during my period of research (see appendix A2).





### 3.2 Development of the proposal for UK Biobank (1998-2000)

#### 3.2.1 MRC/Wellcome Trust Workshop (1998-1999)

The proposal for UK Biobank, or as it was formerly known the UK Population Biomedical Collection, was considered by the MRC and the Wellcome Trust simultaneously during the final years of the HGP in the late nineteen nineties. The MRC included the proposal for a new large scale cohort study in their bid to the 1998 Government Comprehensive Spending Review. The bid stressed the need for ‘large collections of well characterised human DNA samples for research on gene function and the interaction between genetic and environmental risk factors in multi-factorial diseases’ (S600/161 Volume 1). A MRC post-genome challenge working group on DNA sample collections and facilities for large scale genetic typing met on the 29 May 1998. This working group included scientists who went on to undertake important roles in the origins and development of UK Biobank, such as the then head of the MRC George Radda, John Bell,<sup>34</sup> Nick Day,<sup>35</sup> Peter McGuffin,<sup>36</sup> and David Porteous<sup>37</sup> and included other senior academic figures (D Armstrong, G Cameron, S Povey, G Samuels, E Southern and E Wright - the document used initials rather than first names). It defined three types of studies that were needed, including very large case control studies to identify disease genes or disease modifier genes, large longitudinal cohorts to study gene-environment interaction using prospectively gathered information on exposure and lifestyle, and large well documented case series with non-responders and responders identified from within the series to identify genes affecting treatment response (S600/161 Volume 1).

The first official meeting between the MRC and the Wellcome Trust regarding UK Biobank was on the 14 May 1999, at a jointly convened workshop (S600/161 Volume 1). Although I did not have access to material that listed the full attendance at the workshop, certain documents contained such details. It was held at the Royal College of Physicians in London and was attended by representatives of other major UK

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<sup>34</sup>Member of the EWG and Chair of the Science Committee

<sup>35</sup>Member of the EWG and PDC

<sup>36</sup>Led a working group at the Protocol Development Workshop

<sup>37</sup>Member of the EWG and PDC, and led a working group at the Protocol Development Workshop

funding bodies and charities such as Imperial Cancer Research Fund (ICRF),<sup>38</sup> Cancer Research Campaign (CRC), British Heart Foundation (BHF) and British Diabetic Association (BDA). The workshop considered the need for a new large scale population study for research on ‘genetic risk factors for disease, gene/phenotype/environment interactions and infectious diseases’ (S600/161 Volume 1). It reviewed relevant existing cohorts in determining the need for a new one and considered the form a potential study would take. The workshop concluded that it would be worthwhile to set up a study and that the information to be gained from it could not be obtained from existing studies. It recommended the establishment of an expert working group to develop the outline for the resource (S600/161 Volume 1).

The first session was chaired by John Todd<sup>39</sup> and reviewed existing cohorts. It featured presentations from representatives of existing cohort studies in the UK including Jean Golding of the Avon Longitudinal Study of Parents and Children (ALSPAC), Nick Day<sup>40</sup> of the European Prospective Investigation of Cancer (EPIC), Michael Marmot of the Whitehall II and Health Survey for England, David Barker of the Hertfordshire and Southampton Cohorts, Mike Wadsworth of the 1946 and other UK birth cohorts and Steve Humphries of the Second Northwick Park Heart Survey. There was open discussion of the ability of existing cohort studies to ‘meet future needs’ (D550/33 Volume 1). The debate included presentations by senior scientists Walter Bodmer, John Bell and Roy Anderson. The second session was chaired by George Radda and in considering ‘strategies for the future’ featured presentations by Martin Bobrow<sup>41</sup>, David Porteous and Peter Morgan Capner. The workshop ended with an open discussion, a summary and recommendations by George Radda and John Todd (D550/33 Volume 1).

### 3.2.2 Expert Working Group (EWG) (1999-2000)

The EWG was established in May 1999 to consider the justification for a new large scale cohort study and to develop the outline for the resource. It was chaired by Tom

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<sup>38</sup> The Imperial Cancer Research Fund (ICRF) merged with the Cancer Research Campaign (CRC) in 2002, forming Cancer Research UK.

<sup>39</sup> Member of the EWG

<sup>40</sup> Member of the EWG, PDC and a Spoke, and led a working group at the Protocol Development Workshop

<sup>41</sup> Member of the EWG

Meade<sup>42</sup> and the members were David Porteous, John Bell, John Todd, Valerie Beral,<sup>43</sup> Martin Bobrow, Nick Day, Peter Donnelly, Trevor Gibbs, Mark McCarthy<sup>44</sup> and Roy Anderson. There were a number of observers in the group such as Jonathon Gershuny and Alison Nichols from the Economic and Social Research Council (ESRC), Richard Laux and Joanna Brown from the Office of National Statistics (ONS), Peter Greenaway,<sup>45</sup> David Coles and Mark Salmon from the Department of Health, and Alison Spaul from the Scottish Executive (S600/161 Volume 1).

The EWG met four times between August 1999 and January 2000. Included in its terms of reference was a remit to review existing UK population studies and cohorts to determine the extent to which they could meet the need for research on genetic, physiological, lifestyle and environmental risk factors for diseases of significant public health importance, to contemplate the opportunity for extending existing collections, and to develop the outline for a new population study or studies to gather information not available from existing cohorts (S600/161 Volume 1). At its second meeting on the 27 September 1999, the group evaluated current studies and members presented outline proposals to ‘further identify issues to be taken into account in work of the kind they have in mind, including duration and cost as well as type of population(s) needed so that we can be realistic in making recommendations’ (S600/161 Volume 1). These included ‘Outline of a proposed design for a large national cohort study – epidemiological considerations’ by Nick Day, ‘UK Biomedical Collections, Large Prospective Cohort’ by John Bell and Valerie Beral, ‘MRC Working Party, Imperial College Proposal’ by Mark McCarthy, ‘A Vision of Epidemiology Studies of the Future’ by Trevor Gibbs, ‘UK National Resource Collections Research Opportunities in Scotland’ by David Porteous and ‘UK Population Survey (UPS): considerations for a national cohort study’ by John Todd (S600/161 Volume 1). The group considered issues including hypothesis development, sample size and age range, exposure ascertainment, organisation, public acceptability and ethical issues, costs, pharmacogenetics, ownership and acceptability and pilot work in developing an outline for the proposal (S600/161 Volume 1).

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<sup>42</sup> Chair of the PDC

<sup>43</sup> Member of the Science Committee and Spoke Lead

<sup>44</sup> Member of the PDC and a Spoke, and led a working group at the Protocol Development Workshop

<sup>45</sup> Member of the PDC

The EWG published their final report in March 2000. This recommended the establishment of two new UK Population cohort studies: an adult cohort to examine genetic and environmental risk factors and their interaction for common multifactorial diseases of adulthood; and a birth cohort ‘primarily to construct a population profile of exposure and immunological responses to the prevailing common infections in the UK’ (S600/161 Volume 2). It stressed the higher priority of the adult cohort because it would have more of an impact on public health in the medium term, and because it was at a more developed stage of planning. The report stated that the birth cohort would be needed to address common infectious disease, developmental disease or childhood antecedents of adult markers for disease risk. The group also included a list of recommendations in support of the conclusion that a new large prospective study on genetic and environmental risk factors for common adult diseases details should be established. It detailed the debate over the prospective cohort design as opposed to large case-control studies, the management and organisation of the adult cohort study, ownership and accessibility, ethical issues and public acceptability, and public consultation (S600/161 Volume 2). The report was approved by the MRC Council and Wellcome Trust Governors in spring 2000. It was circulated to MRC Research Boards, Wellcome Trust Panels and individual experts for comment prior to further protocol development (S600/176 Volume 1). In June 2000 the MRC and the Wellcome Trust agreed in principle to the proposal for UK Biobank (<http://www.ukbiobank.ac.uk/organisation.html> 2004) (accessed 23/04/04).

### 3.3 Protocol Development and Consultation (2001-2003)

#### 3.3.1 Protocol Development Committee (PDC) (2001)

The PDC was established in May 2001 to ‘steer and oversee’ the production of a detailed draft protocol for a proposed cohort study, and to endorse it in time for international peer review and for passing on to the funding bodies. It was asked to consider the financial constraints involved in UK Biobank and the consultations undertaken with the scientific community, the public, health professionals, industry, and charities that would ‘inform’ the protocol (S600/174 Volume 1).

It met on five occasions between May and December 2001. It was chaired by Tom Meade and the members were Emily Banks (protocol writer), Paul Burton,<sup>46</sup> Nick Day, Anna Dominiczak,<sup>47</sup> Mark Duman, Mark McCarthy, David Porteous, Martin Prince,<sup>48</sup> Anne Richardson, David Strachan,<sup>49</sup> Alan Silman,<sup>50</sup> Ian Purves,<sup>51</sup> Ron Zimmern,<sup>52</sup> Lon Cardon, and, representing the offices of the funding bodies, Alan Doyle (Wellcome Trust), Stephane Goldstein (MRC) and Frances Rawle (MRC). Following the first meeting Peter Greenaway was included as a member representing the Department of Health, and various alterations occurred regarding office staff from the funding bodies (D550/33 Volume 2). The major issues discussed by the PDC in achieving its aims included: the name for the resource, cohort selection and sample size, communication and consultation (including the protocol development workshop), IT strategy, development of hypotheses, proposals for additional studies, recruitment, baseline measures, follow up, statistical methods, pilot studies, ethical considerations, links with other studies, costs, Intensively Phenotyped Cohort (IPC)<sup>53</sup> and the role of the spokes (D550/33 Volume 2).

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<sup>46</sup> Member of the Science Committee, Spoke Lead and led a working group at the Protocol Development Workshop

<sup>47</sup> Spoke member and led a working group at the Protocol Development Workshop

<sup>48</sup> Member of a Spoke

<sup>49</sup> Led a working group at the Protocol Development Workshop

<sup>50</sup> Member of the Science Committee, Spoke Lead and led a working group at the Protocol Development Workshop

<sup>51</sup> Led a working group at the Protocol Development Workshop

<sup>52</sup> Spoke member and led a working group at the Protocol Development Workshop

<sup>53</sup> The IPC was a proposal put forward by the PDC for an additional study involving more intensive phenotyping of a 40,000 subgroup of participants aged between 45 and 54 from the main cohort (S600/176 Volume 1).

Various issues were debated within subgroups of the PDC. For example, a brainstorming meeting on the 21 June 2001 focussed on communication issues such as interaction with the scientific community, the media, interest groups and the public. It was attended by additional members who were largely drawn from the offices of the funding bodies such as Trish Evans from the Wellcome Trust and Jane Gizbert from the MRC (D550/33 Volume 2). A subgroup was also set up to discuss sample size and criteria for cohort selection. It consisted of Emily Banks, Paul Burton, Nick Day and David Strachan and considered power and sample size calculations, and expected number of events on the cohort. It reported to the committee on the 18 July 2001 (D550/33 Volume 2).

A further subgroup was established to develop an IPC. It met three times between August and October 2001, although the initial meeting was introductory and widely attended by members of the committee including Tom Meade and Emily Banks. The membership of the two key meetings consisted of Paul Burton as chair, Lon Cardon, Mark McCarthy, Martin Prince, David Strachan, Alan Silman, Alan Doyle and Frances Rawle. The issues discussed by the subgroup included cost, benefits of the IPC and timing of the development of the IPC protocol in relation to the core protocol. At the fourth meeting of the main committee (an away day on the 19 and 20 October 2001), it was announced that George Radda and Mike Dexter [heads of MRC and Wellcome Trust respectively] had decided that the IPC protocol should be considered separately from the core protocol (D550/33 Volume 2).

The first draft of the protocol was produced by Emily Banks on the 12 October 2001, for discussion at the fourth meeting of the committee. The provisional proposal for the IPC was also produced on the 12 October by Paul Burton for discussion by the full committee. A further draft of the IPC protocol, edited following the away day meeting, was circulated by Mark McCarthy on the 12 November 2001. He was informed on the 15 November that it would be rewritten and shortened by Emily Banks and Frances Rawle, to be circulated to the peer reviewers with a covering letter of recommendation (S600/174 Volume 2).

### 3.3.2 International Peer Review of Draft Protocol (2001-2002)

An international peer review panel was asked to comment on the November 2001 draft of the protocol and the IPC protocol on the 5 December 2001. They were specifically asked to consider international competitiveness, timeliness, design, location and value for money (S600/176 Volume 1). The panel consisted of nine reviewers and their comments varied considerably in length and detail. One reviewer's comments were half a page long, four reviewers' commented in one and a half pages, three were between 3 and 5 pages, and one reviewer responded with 8 pages of comments. The comments were largely of a technical nature but the following broad themes emerged: response rate, age range, exposure assessment and prospective design. Despite the scientific nature of the comments, one reviewer questioned the hub and spoke model that had been proposed. He criticised the proposed role of the spokes as data collectors: 'to do this for up to 10 or more years and not have any control over any of the data presents a problem for even the most senior and enlightened of academic investigators' (S600/176 Volume 1). Another non-scientific issue that emerged in reviewers' comments was criticism of the level of detail contained in the protocol, and one reviewer described it as 'very general' (S600/176 Volume 1). The inclusion of timeliness of the initiative as an area to be considered by reviewers reflects the positioning of the UK Biobank as a response to the 'post-genome' challenge. This is reflected in a reviewer's response to this area: 'with the tools of the human genome project at hand, we are running out of excuses not to perform detailed genetic and genetic-epidemiological analyses of common human diseases' (S600/176 Volume 1).

The funding bodies sought further comments from the international peer review panel in the form of a survey in January 2002. The document pertaining to this survey 'Biobank UK – International Peer Review Process Final Survey Results' lists the questions asked and the reviewers' responses. Seven of the original nine experts responded to this survey. The questions were general in nature and required 'yes/no' style responses. The following questions were asked: 'On balance do you support the rationale for Biobank' (all replied 'yes'), 'Overall, are you supportive of the proposed methodology for Biobank UK' (six of the seven replied 'yes'), 'Over the next five to ten years do you believe that demand for a resource of this nature is likely to... (two



replied ‘stay the same’, five replied ‘increase’ ), ‘Do you believe the UK is a good place to establish such a cohort study’ (six replied ‘yes’ and one replied ‘not sure/don’t know’), ‘Please indicate the degree to which you agree with the following assertion about the proposed Biobank UK initiative...“Biobank UK will make a significant contribution to the resources for genetics research worldwide” ’ (three replied ‘strongly agree’, three replied ‘tend to agree’, one replied ‘tend to disagree’), ‘Please indicate the degree to which you agree with the following assertion about the proposed Biobank UK initiative ...“The Biobank UK project will represent good value for money” ’ (three replied ‘strongly agree’, one replied ‘tend to agree’, one replied ‘tend to disagree’, two replied ‘don’t know’), ‘Please indicate the degree to which you agree with the following assertion about the proposed Biobank UK initiative: “The 45-69 age group is the most appropriate to focus on” ’ (four replied ‘strongly disagree’, one replied ‘don’t know’ and two replied ‘tend to agree’), ‘Are there any specific aspects of the proposed data collection that you think should be re-examined’ (six replied ‘yes’ and one replied ‘no’), and ‘Please use this space for any comments, suggestions or reservations associated with these or other issues’ (S600/176 Volume 1).

Reviewers were also given the opportunity to support their answers and these comments included considerable caveats. Although all respondents said ‘yes’ to ‘On balance do you support the rationale for Biobank’, one reviewer stated that ‘one limitation that should be addressed is the lack of reference to specific environmental pollutants’. Similarly, another added

[B]roadly I welcome the thrust of the study as it is attempting to address key and vital issues. However, I believe the protocol is deficient in certain areas, particularly in some of the practicalities in terms of primary care support, recruitment and retention of volunteers and the ethical considerations of such a study.

Despite replying ‘tend to agree’ to ‘Please indicate the degree to which you agree with the following assertion about the proposed Biobank UK initiative ... “The Biobank UK project will represent good value for money” ’, one reviewer added ‘the study is not strictly necessary, because of the already existing initiatives’. In response to the final request for additional comments, one reviewer stated that UK Biobank was ‘an important initiative’ but added

I am afraid that the proposed research approach is too simple-minded to lead to any meaningful outcome. Fewer but much better phenotyped subjects of all ages and walks of life (including exposure to environmental pollutants) is the lead to be followed. These days the time and effort to code one validated questionnaire far exceeds the means of genotyping. It is time to shift emphasis from robotics to genetically manipulated animal models to research that has direct relevance in the clinical and preventive arena.

The 'yes/no' style responses to these questions were tabulated in a further document 'A tabulation of reviewers' comments incorporating preliminary and final comments, Biobank UK, January 2002'. This table stated that 8 of the reviewers were supportive of the rationale and methodology and one was supportive of rationale but not the methodology. This table did not contain the reviewers' additional comments that supported their initial response and therefore did not fully portray the response to the original survey (S600/176 Volume 1).

The PDC considered the peer reviewers' initial comments on the 21 December 2001. Their response largely concerned the proposed age range and prospective cohort approach as opposed to case-control study approach (S600/174 Volume 2). The protocols were sent to the MRC board (the document does not specify which MRC Board) on the 22 February 2002, in preparation for the funding decision meeting in March 2002 (S600/176 Volume 1).

### 3.3.3 Consultation (2001-2003)

Consultation exercises with a variety of groups including industry, interest groups, scientists, health workers, general practitioners and the public were undertaken by the funding bodies directly, and by research groups and consultancies on their behalf between 2001 and 2003.

The funding bodies consulted industrial groups to understand how they would use the resource and obtain their views on the proposed access arrangements. Such consultation included individual meetings, teleconferences and industry-wide workshops with pharmaceutical companies. For example, there was a meeting

organised by the Bio-Industries Association (BIA)<sup>54</sup> at the request of the MRC and the Wellcome Trust on the 26 September 2001. It was attended by Alan Doyle, Frances Rawle and Peter Greenaway on behalf of the funding bodies, Alison Campbell from MRC Technology (MRCT)<sup>55</sup> and representatives from various pharmaceutical companies including Oxford Biomedica and Canitech, Oxagen and Oxford Glycosciences (A156/12 Volume 1). Teleconferences took place with CARTaGENE on the 21 November 2001 (S600/176 Volume 1) and GlaxoSmithKline on the 27 November 2001 (A156/12 Volume 1). There was a meeting between representatives of the funding bodies and Pfizer on the 15 January 2002 (A156/12 Volume 1).

A Consultation with Industry Workshop took place on the 30 and 31 October 2002 at the Hinxton Hall Conference Centre. Although the full attendance was not listed on the documents accessed, pharmaceutical companies such as GenoMed and Calltech were invited. It focussed on access arrangements, Intellectual Property Rights (IPR), management, ethics and governance and protocol development. It included presentations by Martin Bobrow, John Bell, Tom Meade, Alison Campbell, Frances Rawle and Alan Doyle (A156/12 Volume 1). Another consultation with industry workshop, organised by the funding bodies, took place on the 4 April 2003 at the Association of the British Pharmaceutical Industry (APBI)<sup>56</sup> head office in London. Again, the full attendance was not listed on the document accessed but it did reveal that Richard Tiner (head of APBI) acted as chair, an introduction was presented by John Newton as the newly appointed CEO of UK Biobank and representatives of the funding bodies such as Frances Rawle, Alan Doyle and Alison Campbell (MRCT) each gave presentations. It took the form of a question and answer session relating to the issues presented including features of UK Biobank, management structure and ethics and governance and IPR and access arrangements (<http://www.ukbiobank.ac.uk/consultation.html> 2004)(accessed 23/04/04).

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<sup>54</sup> The BioIndustry Association, established in 1989, is the trade association for enterprises in the UK's bioscience sector ([http://www.bioindustry.org/cgi-bin/contents\\_view](http://www.bioindustry.org/cgi-bin/contents_view) 2006) (accessed 14/02/06)

<sup>55</sup> MRCT is the 'exclusive commercialisation catalyst for the UK Medical Research Council (MRC) working to translate cutting edge scientific discoveries into commercial products' (<http://www.mrctechnology.org/home.html> 2006) (accessed 14/02/06).

<sup>56</sup> The Association of the British Pharmaceutical Industry (APBI) is the trade association for approximately one hundred companies in the UK producing prescription medicine (<http://www.abpi.org.uk> 2006) (accessed 14/02/06).

Consultation with interest groups largely took the form of meetings between representatives of the funding bodies and the Human Genetics Commission (HGC),<sup>57</sup> which occurred between 2001 and 2004. The HGC considered the proposal for UK Biobank in its report on the storage, protection and use of personal genetic information in 2002 (S600/176 Volume 1). A HGC Information Gathering Meeting on the UK Biobank took place on the 19 November 2002. It was attended by members of the Commission, representatives from the Office of Science and Technology,<sup>58</sup> the House of Commons Science and Technology Select Committee,<sup>59</sup> the Genetics Interest Group,<sup>60</sup> and Human Genetics Alert.<sup>61</sup> The issues discussed included the draft protocol, the scientific rationale behind UK Biobank, oversight and governance, consent, confidentiality and data storage, commercial access to Biobank data and IPR (A156/12 Volume 1). As UK Biobank progressed the HGC continued to be consulted and updated on its progress. For example, a meeting with the HGC Genetics Sub-group on the 18 June 2003 included representatives from UK Biobank, such as the then CEO John Newton and the chair of the Interim Advisory Group (IAG), William Lowrance, as well as representatives of the funding bodies and members of the HGC Genetics sub-group. The focus of the meeting was the progress made in establishing UK Biobank, commercial use and impact on MRC and Wellcome Trust budgets, the role of the IAG and development of the Ethics and Governance Framework (EGF) (D550/19 Volume 1). A further update meeting with the HGC occurred on the 30 March 2004, which particularly concerned the Intellectual Property (IP) and access policy and the Ethics and Governance Council (EGC). Presentations were given by representatives of UK Biobank and the funding bodies. John Newton discussed

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<sup>57</sup> The HGC is the 'Government's advisory body on human genetics, particularly social, ethical and legal issues' (<http://www.hgc.gov.uk/Client/index.asp?ContentId=1> 2006) (accessed 14/02/06).

<sup>58</sup> The Parliamentary Office of Science and Technology (POST) is the 'UK Parliament's in-house source of independent, balanced and accessible analysis of public policy issues related to science and technology' ([http://www.parliament.uk/parliamentary\\_offices/post.cfm](http://www.parliament.uk/parliamentary_offices/post.cfm) 2006) (accessed 14/02/06).

<sup>59</sup> The House of Commons Science and Technology Committee examines 'the expenditure, administration and policy of the Office of Science and Innovation and its associated public bodies' ([http://www.parliament.uk/parliamentary\\_committees/science\\_and\\_technology\\_committee/about\\_the\\_committee.cfm](http://www.parliament.uk/parliamentary_committees/science_and_technology_committee/about_the_committee.cfm) 2007) (accessed 16/02/07).

<sup>60</sup> The Genetics Interest Group is a 'national alliance of patient organisations with a membership of over 130 charities which support children, families and individuals affected by genetics disorders' (<http://www.gig.org.uk> 2007) (accessed 16/02/07).

<sup>61</sup> Human Genetics Alert is an 'independent public interest watchdog group opposed to certain development in genetic research such as genetic discrimination, cloning and inheritable genetic engineering of human beings' (<http://hgalert.org> 2006) (accessed 14/02/06).

progress, Jo Sumner from the MRC spoke about the EGC and Tara Camm from the Wellcome Trust discussed IP and access issues (D550/19 Volume 1).

The most significant consultation exercise undertaken with the scientific community was the Protocol Development Workshop on the 17 April 2001 at the Royal College of Physicians. A total of 180 delegates attended the workshop. The first session featured workshops on technical and practical issues. There was a workshop on Blood Samples: Collection, Extraction, Storage and Analysis led by David Porteous, Cohort Selection and Recruitment led by Paul Burton, Information Technology: Data Collection and Databases led by Ian Purves, Measuring diet data led by Sheila Bingham, and Ethics: Consent and Feedback led by Ron Zimmern. The second session was a series of working groups on baseline data collection and outcome measures. There was a working group on Cardiovascular Disease led by Anna Dominiczak, Diabetes and Metabolic Disorders led by Mark McCarthy, Respiratory/Infection led by David Strachan, Mental Health/Neurology led by Peter McGuffin, Cancer led by Nick Day, and Musculoskeletal led by Alan Silman. The majority of the workshops and working groups were led by members of the PDC. A report of the workshop was written by Frances Rawle and a number of responses were made to it in October 2001, such as responses from Valerie Beral, Sheila Bingham, Jean Golding (the then head of ALSPAC) and Stephen Palmer (D550/33 Volume 2).<sup>62</sup>

Consultation with the public, health workers and general practitioners was undertaken by research groups and consultancies on behalf of the funding bodies between 2000 and 2003.

The research consultancy company, Craig Ross Dawson, was commissioned by the MRC and the Wellcome Trust to ‘explore public attitudes to the use of human biological samples and linkage of the information extracted from them to medical database information’ (<http://www.ukbiobank.ac.uk/docs/perceptions.pdf> 2004) (accessed 23/04/04). They undertook fieldwork between March and April 2000 and published their report ‘Public Perceptions of the Collection of Human Biological Samples’ in October 2000. Sixteen focus groups were undertaken with members of

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<sup>62</sup> Member of the Science Committee and Spoke Lead

the general public and in-depth interviews were carried out with general practitioners, practice nurses, people who experienced disease or disabilities, religious and community leaders, and representatives of interest groups (<http://www.ukbiobank.ac.uk/docs/perceptions.pdf> 2004) (accessed 23/04/04).

A consultation event with primary health care professionals from the Trent Focus Collaborative Research Network was undertaken by the Genetics Interest Group (GIG) and the Universities of Nottingham and Sheffield on behalf of the funding bodies in October 2000. It was undertaken to discover any potential obstacles in primary care to the operation of UK Biobank. It involved twenty-six individuals from twenty-three practices, allocated to five focus groups. The topic areas were attitudes to research, awareness of the proposed MRC and Wellcome Trust Research, recruiting subjects and obtaining consent, data collection and access to data. The report 'Consultation with primary health care professionals on issues relating to the recruitment of patients to a DNA collection study' was published in January 2001 (<http://www.ukbiobank.ac.uk/docs/GPreport.pdf> 2004) (accessed 23/04/04). Between January and April 2003 GIG, in collaboration with the North Thames GP Research Network (NoCTEN), also organised a consultation dinner with London based GPs, and a total of eighteen GPs attended (<http://www.ukbiobank.ac.uk/docs/GPreport.pdf> 2004) (accessed 23/04/04).

In 2002 People, Science and Policy (PSP) (an independent science policy consultancy) were commissioned by the MRC and the Wellcome Trust to undertake consultation with the public on the ethical and management issues surrounding UK Biobank. Three sessions were held in January 2002 in Hertfordshire, the West Midlands and Glasgow. Each session involved twenty people aged between 45 and 69, separated into two groups of ten. Following an introductory session of one hour and a half, groups were reconvened at a later date for a four hour interactive workshop with PSP moderators and two representatives from the funding bodies. Their report, 'Biobank UK; A Question of Trust: A consultation exploring and addressing questions of public trust' was published in March 2002 (<http://www.ukbiobank.ac.uk/docs/consultation.pdf> 2004)(accessed 23/04/04). Between January and April 2003 PSP undertook further consultation on behalf of the funding bodies with individuals from social groups under-represented in the initial

2002 consultation. Four groups consisting of a total of twenty-seven people were convened for two hour sessions in Manchester, London, Newport and Northallerton (<http://www.ukbiobank.ac.uk/docs/consultation.pdf> 2004)(accessed 23/04/04).

PSP were again commissioned by the MRC and the Wellcome Trust in 2003 to undertake consultation exercises with nurses, both in general practice and research. Their views were sought to inform the communications strategy and assist the development of UK Biobank, particularly regarding ethical and management issues. One and a half hour sessions were conducted with GP nurses and research nurses separately in February 2003 in Manchester, Glasgow, London, and Birmingham. Further sessions with GP nurses were also held in Worcester, Newport, York, and Hertfordshire. A total of seventy-three nurses were involved in twelve groups. An in-depth interview was carried out with a representative of the Royal College of Nursing (RCN). The report, 'UK Biobank: A consultation with nurses in general practice and research' was published in April 2003 (<http://www.ukbiobank.ac.uk/docs/Nursesreport.pdf> 2004) (accessed 23/04/04). In 2003 PSP were commissioned by the funding bodies to establish a public panel. They set up a panel of sixty-four lay people aged 45-69 from individuals who had previously taken part in consultation sessions about UK Biobank. It was consulted by the IAG on the draft EGF between May and June 2003, prior to the completion of their report and with the support of the funding bodies. It involved two two-hour sessions; forty-seven members attended the first session and forty-two attended the second. The report 'UK Biobank Consultation on the Ethical and Governance Framework' was published in June 2003 (<http://www.ukbiobank.ac.uk/docs/people-science-policy.pdf> 2004)(accessed 23/04/04).

An Ethics Consultation Workshop was organised by the funding bodies on the 25 April 2002, the report of which was published in September 2002. It involved sixty invited individuals from various fields including biomedical scientists, clinicians, social scientists, ethicists, lawyers, health service professionals, patients' groups, and other civil society groups. It featured five working groups which focussed on a specific set of ethical issues namely consent, confidentiality, security, commercialisation, and governance (<http://www.ukbiobank.ac.uk/docs/ethicswork.pdf> 2004) (accessed 23/04/04).

Further consultation regarding the EGF was conducted on behalf of the funding bodies by Opinion Leader Research (a research based consultancy). They organised two day long workshops in May 2003. The first involved members of the public and health practitioners amounting to thirty-nine people. The second engaged a variety of stakeholders with previous involvement in consultation exercises including patient groups and other civil society group members, scientists, social scientists, ethicists, clinicians, lawyers, health service professionals, and those involved in the development of the protocol, amounting to seventeen people. Four in-depth interviews with politicians were also carried out. Their report 'Summary of the UK Biobank Consultation on the Ethics and Governance Framework was published in August 2003 (<http://www.ukbiobank.ac.uk/docs/public-stakeholder-olr-report.doc> 2004) (accessed 23/04/04).



### **3.4 Funding Decision (2002)**

The decision to fund UK Biobank was taken by the MRC and the Wellcome Trust in March 2002. The funding decision was initially to be taken in February 2001 but it was postponed until the production of a full protocol and detailed costing (S600/161 Volume 3). As this chronology is based on information gathered from MRC documents on the origins and development of UK Biobank, my description concerns the process by which the MRC came to the funding decision.

#### **3.4.1 MRC Funding Decision (2002)**

The MRC took the decision to fund UK Biobank at a meeting on the 27 March 2002 of its Council, which was asked to provide enough money to cover half the projected costs of the initial set up and recruitment. The Council also took the decision not to include funds for the IPC in the core funding provided.

In taking these decisions they discussed the following issues: the scientific case, the high national and international profile of UK Biobank and the strong level of government support, the medium and long term financial implications for the MRC of supporting it, the potential impact of the project in improving the ability to use NHS electronic records in future clinical, epidemiological and public health research, the potential implications for improving public understanding of genetics and genetics research, and the future Council oversight of UK Biobank. The endorsement of the MRC Inter Board Initiatives Group (IBIG) for the core protocol was considered, as was their conclusion that the IPC should not be part of the core funding for the resource. Issues raised by IBIG were also considered such as their concern over the staffing of UK Biobank (pointing out that only the protocol writer worked full-time on UK Biobank and on a short term secondment basis). IBIG stressed the importance of appointing a CEO and senior scientific and IT staff for the hub in getting UK Biobank started.

The Council was provided with various materials in making the decision. For example, this included an operational plan that detailed issues including stakeholder acceptability and consultation, management structure, access and IP, ethical and legal

issues, IT, finance, future development (such as hub and spoke selection and CEO appointment), and risks (non financial). A stakeholder analysis document detailed consultations with the public, GPs and other health care professionals, science community, HGC and government departments. The Council was also provided with the minutes of the IBIG meeting on the 4 March 2002 (S600/176 Volume 1).

### 3.5 Internal Organisation in the Funding Bodies (2000-2003)

Various groups were involved in the setting up and development of UK Biobank within and between the funding bodies. Again, this description largely concerns internal organisation in the MRC.

#### *IBIG*

One such group within the MRC was the Inter Board Initiatives Group (IBIG), which consisted of senior figures within the MRC (Board and Council members) such as George Radda, John Bell, Doug Easton, Carol Dezateux, Ray Fitzpatrick, Nancy Rothwell, Karen Steel, Doreen Cantrell, Eve Johnstone, Ian MacLennan, and Patrick Sissons. Its key role in the development of UK Biobank was to advise Council on whether or not to fund the resource.

IBIG met on the 4 March 2002 to consider the scientific case for UK Biobank and review the comments of the peer review panel to allow them to make a recommendation to Council for the funding decision meeting on the 27 March 2002. It recommended that UK Biobank should be funded but that the IPC should not be part of the core MRC funding because the ‘case was not sufficiently strong that this would be an essential component’ (S600/176 Volume 1). Representatives of the EWG, the funding bodies and the international peer review panel were invited to attend the meeting namely Tom Meade, Emily Banks, Alan Doyle, Isaac John (DoH) and three reviewers by audio link. There was a presentation of the initiative from Tom Meade, comments from the referees, a discussion between Tom Meade and Emily Banks, and confidential discussions between IBIG members. The presentation by Tom Meade included comments on the IPC proposal stating that it was important but should not be included in the core funding on account of the cost involved. The referees’ comments concerned the debate over the prospective cohort design as opposed to the case control study approach, the value of the IPC and the age range. The discussion between Tom Meade and Emily Banks reflected the issues raised by IBIG including the scale of the proposal, hub and spoke model, environmental exposures, and public acceptability. The issues raised in the confidential discussions between IBIG members included the lack of detailed costing in the proposal,

timescale, recruitment target, management and accountability rights, and the importance of giving research incentives to spokes (S600/176 Volume 1).

### *HOPB*

Another internal MRC group involved in the development of UK Biobank was the Head Office Project Board (HOPB), which consisted of Nick Winterton as chair, Frances Rawle, Jane Lee, Stephane Goldstein, Don Brunston, Alison Campbell, Diana Dunston, Jane Gizbert, Kevin Moreton, and Ian Viney. The evidence suggests that the group met between 2000 and 2002, with records of the sixth meeting on the 25 February 2001 and another on the 8<sup>th</sup> of January 2002 (S600/176 Volume 1). It considered a range of issues relating to the establishment of UK Biobank including interaction with IBIG and Council regarding the funding decision meeting, consultations, ethical review, legal issues, financial issues, overall project planning post funding decision, planning for different potential outcomes, infrastructure issues such as the hub and spoke bidding process, appointment of committees and the CEO (S600/176 Volume 1), and the funding commitment of the Wellcome Trust (D550/15 Volume 2).

### *JFAT*

A further group involved in the set up of UK Biobank, the Joint Funders Action Team (JFAT), encompassed all the main funding bodies. It was composed of representatives from the offices of the three major funding bodies. Although its precise membership altered from meeting to meeting it generally involved Frances Rawle, Alan Doyle, Stephane Goldstein, Peter Greenaway, Jane Lee, and Karen Shaw. It met between September 2000 and March 2003. Evidence would suggest that the group was responsible for developing UK Biobank until the establishment of the hub in March 2003, although the precise terms of reference were not available in the material I accessed. It addressed key issues including the funding decision, the development of the hub and spoke model including spoke incentives, the relationship between the hub and the spokes, (including financial relationship and the grant versus contract debate) (D550/13 Volume 1) and the role of the various committees including the PDC (D550/15 Volume 2).

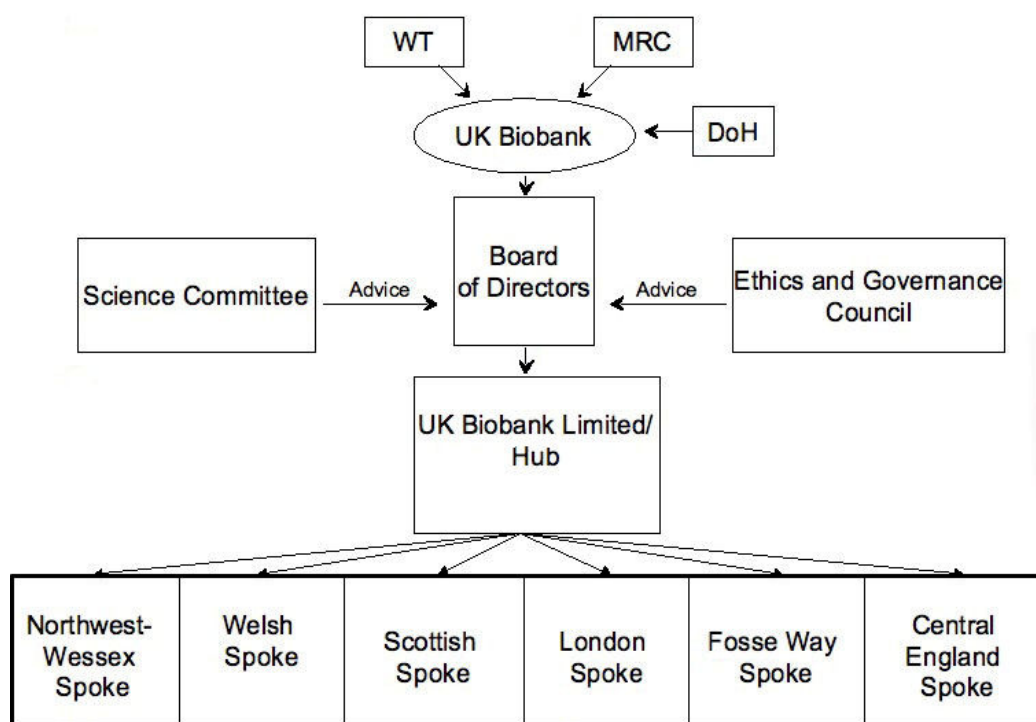
JFAT produced a report on the 14 April 2003, 'UK Biobank Project, Set-Up Stage Lessons Learned Report', to assist in the future development of UK Biobank or other projects undertaken by the funding bodies. It addressed issues surrounding the establishment of UK Biobank including the organisational structure concluding that the 'unique nature of the UK Biobank project being a tri-partite venture aimed at setting up a fourth and independent company may never be repeated', and the adoption of the EU Procurement Rules in the selection of the spokes was described in the report as a 'mistake' (D550/18 Volume 1).

### 3.6 Implementation of the Organisational Structure (2003-2005)

#### *Introduction*

I will now provide a brief overview of the organisational structure of UK Biobank prior to detailing its chronological development. The funding bodies selected an organisational structure that consisted of three main committees and a hub and spoke model. They implemented this organisational structure over several years between 2002 and 2005. The main committees were the Board of Directors (BoD), the Science Committee and the EGC. The hub was also known as UK Biobank Limited and the Central Co-ordinating Centre (CCC), and the spokes were also known as Regional Collaborating Centres (RCCs).

**Diagram 2: Organisational Structure**



The hub, based in Manchester, had overall responsibility for delivering UK Biobank including financial management and storage of the data and samples, and it co-ordinated the activities of the six spokes: the spokes were Scotland, Wales, North West and Wessex, Central England, Fosse Way, and London. The spokes were responsible for recruitment and initial data and sample collection and a total of 22

universities were involved in the consortiums that formed them. These consortiums involved a wide range of academic scientists from various disciplines. The hub was responsible to the BoD, who were in turn accountable to the funding bodies. The scientific protocol was developed by the Science Committee, who served an advisory role to the Board. The EGC was responsible for the development of the EGF and advised the BoD on its implementation (<http://www.ukbiobank.ac.uk/organisation.html> 2004) (accessed 23/04/04).

I have divided this section into two parts; the first focuses on the ‘hub’ and ‘spoke’ model and its implementation, and the second describes the establishment of the main committees.

### 3.6.1 The ‘hub’ and ‘spoke’ model (2002-2005)

The organisational structure originally adopted for UK Biobank was the ‘hub’ and ‘spoke’ model. Although this terminology changed in 2004 when the hub (also known as UK Biobank Limited) became the Central Coordinating Centre (CCC) and the spokes became Regional Collaborating Centres (RCCs), I will use the original terms. The ‘hub’ and ‘spoke’ model was one of the most problematic issues in the origins and development of UK Biobank. I will address the issues involved in the implementation of this model throughout the findings chapters.

#### *3.6.1 (a) Hub and Spoke Selection (2002-2003)*

The first meeting regarding the hub and spoke bidding process was in July 2002 between representatives of the funding bodies and organisations interested in becoming the hub or a spoke (D550/12 Volume 1). The hub was not involved in spoke selection. The funding bodies adopted EU Procurement Rules in the hub and spoke bidding process that forbade applicants from discussing bids.

#### *Hub Selection*

The bidding process for the UK Biobank hub formally began on the 28 October 2002, when representatives of the funding bodies, Frances Rawle, Alan Doyle and Peter Greenaway, sought expressions of interest by the 15 November 2002. The Pre

Qualifying Questionnaire (PQQ) included questions on administrative and sample storage location, academic host, track record, IT facilities, links with regional development authorities and costing for both administrative locations, and IT suite. Ten consortiums bid to be the hub: Cranfield, Bath, Nottingham, White Rose, Cambridge, Oxford, Birmingham/Warwick, Manchester, London, and the International Centre for Life at the University of Newcastle. The bidders were informed of the outcome of the first round process on the 9 January 2003 by Frances Rawle, Alan Doyle and Peter Greenaway. The following six bidders were short listed at this stage: Cambridge, Oxford, Birmingham/Warwick, Manchester, London, and the International Centre for Life. The Cranfield, Bath, Nottingham and White Rose bids were unsuccessful (D550/12 Volume 1).

Site visits were arranged with each of the successful bidders and they were given information about the presentations required (D550/12 Volume 1). Visits were conducted in January and February 2003. The Visit Team consisted of Alan Doyle, Peter Greenaway, Frances Rawle and further representatives from the offices of the funding bodies: Elizabeth Shaw from the Wellcome Trust and David Sonntag and Keith Tucker from the MRC. Following the site visits Manchester was chosen as the hub and the second round bidders were informed of this decision on the 17 March 2003 by Mike Dexter, Peter Greenaway and George Radda. The unsuccessful bidders were given limited feedback on the grounds that further detail of how the bids compared was confidential (D550/12 Volume 1). Manchester was asked to confirm acceptance by the 28 March 2003, enter into negotiations and attend a press conference. They were informed that their selection was confidential until the press conference. The second choice for the location of the hub was Oxford, also notified on the 17 March 2003 (D550/12 Volume 1).

### *Spoke Selection*

Thirteen consortiums were involved in the first round bidding process to become UK Biobank spokes: Cambridge, Fosse Way, North West, London, Wales, MRC General Practice Research Framework (GPRF), Scotland, North West/Wessex, North, Central England, West Midlands, Belfast, and Teddington. Ten were successful in making it through to the second round, with the West Midlands, Belfast and Teddington bids unsuccessful. Each of the first round bidders were sent a pre-qualification



questionnaire (PQQ) to be returned on the 13 November 2002. The questions concerned basic information about organisation, eligibility, economic and financial standing, technical ability, health and safety, and conflict of interest (D550/13 Volume 1). Letters from Frances Rawle, Alan Doyle and Peter Greenaway were sent to the successful first round bidders on the 21 November 2002. They were also sent an Invitation to Negotiate (ITN) and informed that the bids were confidential, and should not be discussed between consortiums (D550/13 Volume 1).

The Spoke Selection Panel was formed in February 2003. It consisted of a former Chief Medical Officer (CMO) for England Sir Kenneth Calman as chair, Mike Dexter, George Radda, Peter Greenaway, John Newton (as CEO designate prior to his formal appointment in March 2003), representatives from MRC Council Peter Fellner, Alan North and Nick Winterton (Executive Director), Wellcome Trust Governors Sir Michael Rutter and Edward Walker-Arnott and three representatives of the international peer review panel (D550/13 Volume 1). They considered the strength of consortium, local management, ability to deliver on recruitment, geographic and population coverage, contribution to the overall Biobank enterprise, and value for money. Further selection criteria included technical issues (recruitment and collection of biological samples), accommodation, financial issues (price of delivering the services per head of recruits), and legal issues (acceptance of draft contract proposals). Representatives of each of the ten second round bidders met with the panel in London for one hour on the 25 and 26 February 2003. The four unsuccessful second round bidders were Cambridge, North West, MRC GPRF and North, and the six successful spoke bidders were London, Wales, Scotland, Central England, North West and Wessex, and Fosse Way. The bidders were informed on the 17 March 2003 in a letter from Mike Dexter, George Radda and Peter Greenaway. The letter to the successful bidders included acceptance terms and a list of non-negotiable issues on which their selection was conditional, including access terms such as the stipulation that there would be no preferential or early access to the resource for spokes (D550/13 Volume 1).

### *3.6.1 (b) Implementation of the hub and spoke model (2003-2005)*

#### *Establishment of the hub*

John Newton was appointed CEO of UK Biobank Limited by the funding bodies in March 2003. He came from the Unit of Health Care Epidemiology, Department of Public Health and Primary Care at the University of Oxford. He was a Consultant Epidemiologist and Director of Research and Development at the Oxford Radcliffe Hospitals NHS Trust. John Newton made his first appearance as CEO on the 7 April 2003 at a Parliamentary and Scientific Committee event at Portcullis House (<http://www.ukbiobank.ac.uk/why.html> 2004) (accessed 23/04/04).

UK Biobank was incorporated as a private company limited by guarantee on the 28 November 2003. The company, UK Biobank Limited, was registered as a charity with the charity commission on the 30 December 2003. The members of the company were the MRC and the Wellcome Trust. A Joint Venture Agreement (JVA) was completed on the 29 January 2004 between the members of the company (Wellcome Limited as a trustee of the Wellcome Trust and the MRC) and UK Biobank Limited. The agreement was subject to a number of drafts, the first completed on the 13 December 2002, the third on the 26 June 2003 and the fifth on the 14 October 2003. The JVA included the following sections: purpose of the company and project phases, financial matters, IP and access, obligations of the parties, costs, and conflict with articles. It detailed arrangements for the monitoring and assessment of the pilot phase. The criteria for judging the pilot phase included successful recruitment, the collection of high quality data from the NHS on the health outcomes of participants, the completion of recruitment on time and in budget, the secure and efficient collection and storage of data, and the members' agreement of the revised protocol. The arrangements for the contribution of the DoHare detailed and the agreement was made that it would be given via the MRC (D550/17 Volume 1).

#### *Establishment of the hub and spoke relationship*

Representatives from the hub and the spokes met in Manchester on the 20 May 2003 with representatives of the selection panel and the funding bodies to discuss the way forward, specifically regarding the contact between the hub and the spokes. The following issues were discussed: funding add-on studies, oversight body, function of

consortia in spokes, and communication. A RCC negotiating team was formed to discuss costs, non-negotiable issues in the letter of award and issues raised by them, and the evidence suggests they met on the 23 July 2003 (D550/10 Volume 1). Negotiation regarding the contract continued between 2003 and 2004 and UK Biobank released pre-contract funding for each of the spokes on the 26 March 2004, covering costs up to the value of £80,000 (D550/10 Volume 1). The evidence suggests that a draft contract formulated in December 2002 was amended following the issues raised by the spokes and other developments (such as the spokes becoming RCCs and the Oversight Body becoming the EGC) and circulated to the spoke leads from Tara Camm of the Wellcome Trust on the 8 April 2004. The description of the document changed and the April 2004 draft was described as a 'Research Services Agreement'. The spokes responded to this draft on the 30 April 2004 and negotiation continued throughout 2004 but contracts were never signed during my period of research (D550/10 Volume 1).

#### *Implementation of the hub and spoke model in the Phase One Pilot Study*

The Phase One Pilot Study began in Nottingham on the 28 February 2005, following approval from the North West Multi-centre Research Ethics Committee (MREC). Further pilot studies ensued in Aberdeen, Manchester, Edinburgh, London, Oxford and Wales. These pilot studies were carried out to determine how a visit to a UK Biobank assessment centre would work and they recruited approximately 300 volunteers in total. Various science committee subgroups recommended changes to the protocol for the phase one pilot studies, including new questions on diet, mental health, environmental exposures, a new heart measurement, and participants being offered a record of the measurements taken during the visit. Volunteers, largely from medical and university communities, answered lifestyle questions using a touch-screen questionnaire and had their blood pressure, lung function, body fat, height and weight measured. (<http://www.ukbiobank.ac.uk> 2005) (accessed 10/11/05).

### 3.6.2 Establishment of Committees (2003-2004)

#### *IAG (2003)*

The IAG was established in February 2003 by the funding bodies to advise them on the development of the EGF. The members of the group were William Lowrance as

chair, Alastair Campbell,<sup>63</sup> Erica Haines, Graeme Laurie,<sup>64</sup> Chris Mathew, Jean McHale, Onaora O'Neill, Helen Millar, Madeline Wang, and representatives from the funding bodies such as Joanne Sumner, Tara Camm, Alan Doyle, Peter Greenaway, Jane Lee, Nancy Lee, Elizabeth Mitchell, Frances Rawle, Keith Preece, and Martin Sexton (see Appendix A2 for members' biographies). The representatives from the offices of the funding bodies changed over time. Representatives from UK Biobank, for example John Newton (the then CEO) and John Bell (Chair of the Science Committee), were invited to attend some of the meetings as observers.

The IAG met three times between February 2003 and July 2003, with the second and third meeting spanning two days. In advising the funding bodies on the development of the EGF, the group debated a wide range of ethical, legal and social issues. These included consent, confidentiality and security, consultation, access to and use of data and samples, governance, recruitment, organisational structure, expectation of profit-making use and IPR licensing and revenue-sharing arrangements, ongoing dialogue with participants, feedback, expectation of re-contact, right to withdraw, respect for incapacitated and deceased participants, contingency in the event of closure and adoption, implementation, and revision of EGF (D550/7 Volume 2). Documents were circulated to assist discussions. These included working drafts of the EGF, a note from John Newton on consent procedures and data flows for UK Biobank (25 March 2003), a working draft on IPR and access arrangements (28 March 2003), a document on the relative merits of company and committee structure by Tara Camm from the Wellcome Trust (18 March 2003), and a comparison of the consent forms used by projects comparable to the UK Biobank (for example the consent forms used in the ALSPAC cohort study) (D550/7 Volume 1). The group was informed of the consultation exercises undertaken on behalf of the funding bodies, such as the Ethics Consultation Workshop in April 2002, which they took into account in advising the funding bodies (D550/7 Volume 2). The third meeting of the IAG was attended by representatives from the consultancy firms, including Opinion Leader Research and People, Science and Policy, acting as observers for discussion of their reports. The IAG prepared a document on the 10 October 2003 detailing the background to and explanation for key aspects of Version 1.0 of the EGF.

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<sup>63</sup>Chair of EGC

<sup>64</sup>Member of the EGC

The EGF was prepared and developed by the funding bodies with the advice of the IAG. William Lowrance and Jo Sumner were responsible for putting the draft framework together. It went through many drafts such as version 0.3 of the 7 May 2003 and version 0.4 of the 25 June 2003 (D550/7 Volume 1). The final draft (version 1.0) was completed on the 15 August 2003. It was circulated amongst the group on the 19 August allowing for amendments to be made. It was published on the 24 September 2003 for a one month period of open public comments, following which it was revised, approved by the funding bodies and passed on to the BoD (D550/7 Volume 2). The EGF was produced to ‘set standards’ for UK Biobank, and to ensure that the necessary safeguards were in place for the data and sample to be used for scientifically and ethically approved research only (<http://www.ukbiobank.ac.uk/ethics.html> 2004) (accessed 23/04/04).

#### *Science Committee (2003)*

The Science Committee was established in July 2003. It was partly composed of the six spoke leads, a representative from social science and a ‘lay’ representative. The members were John Bell as chair, Valerie Beral, Paul Burton, John Danesh, Paul Elliot, Hilary Graham, Bernard Keavney, Stephen Palmer, Catherine Peckham, Jill Pell, Mike Pringle (deputy chair), Alan Silman, John Todd and Madeleine Wang (see Appendix A2 for members’ biographies). Its role was to advise the BoD on the protocol, the direction and scientific goals of UK Biobank, and review the protocol (<http://www.ukbiobank.ac.uk/science.html> 2004)(accessed 23/04/04). The Science Committee was advised by an Integration Group, composed of the six spoke leads and the chair, on the progress and implementation of pilot studies.

Six Science Committee subgroups were set up to develop the procedures for conducting UK Biobank and report to the Integration Group on the development of the scientific strategy. The questionnaire subgroup, chaired by Rory Collins (Central England spoke member), was responsible for developing the participant questionnaire, and three short-term subgroups advised it on different measurements: environment (chaired by David Coggan, London spoke member), diet (chaired by Stephen Palmer, Welsh spoke lead) and cognition/psychological outcomes (chaired by John Gallacher, Welsh spoke member). The measurement subgroup, chaired by Paul

Elliot (London spoke member), was responsible for advising on the physical measurements to be undertaken, and a repeat measures subgroup, chaired by Paul Burton (Fosse Way spoke member), reported to it. The recruitment subgroup, chaired by Alan Silman (North West spoke member), advised on the recruitment models being tested. The ethnic minorities subgroup, chaired by Mark Caulfield (London spoke member), advised on the recruitment and retention of ethnic minority groups. The longitudinal follow-up subgroup, chaired by Mike Pringle (Fosse Way spoke member and deputy chair of Science Committee), advised on the longitudinal follow up using routine data sources and the validation of exposures and outcomes. The resource stewardship subgroup was not fully established during my period of research but it was proposed that it would be chaired by John Bell and responsible for advising on the management of and access to the resource. An Assessment Centre Delivery Team (ACDT), chaired by Anna Hansell (London spoke coordinator), planned the assessment centre roll-out. It reported to Tim Sprosen at the hub and implemented the strategy agreed by the Integration Group and Science Committee (<http://www.ukbiobank.ac.uk> 2005) (accessed 10/11/05).

#### *BoD (2004)*

The BoD was established in January 2004. It was partly composed of representatives from the three major funding bodies, the science committee, the host of the hub and a lay representative. It consisted of Alan Langlands as chair, John Bell, Peter Benson, Jane Lee, Mike Pringle, Barbara Skene, David Gordon and Marc Taylor (see Appendix A2 for members' biographies).<sup>65</sup> The Board was accountable to the members of UK Biobank Limited (MRC and Wellcome Trust) and acted as company directors and charity trustees. It was responsible for the overall direction, management and control of UK Biobank Limited, and had three committees: science committee, audit committee and the remuneration committee. The first meeting was on the 29 January 2004 in which it agreed the terms upon which the MRC and the Wellcome Trust would provide funding for UK Biobank (<http://www.ukbiobank.ac.uk/organisation.html> 2004) (accessed 14/09/04).

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<sup>65</sup> Marc Taylor replaced Peter Greenaway who retired from the DoH in July 2004

*EGC (2004)*

The EGC was established in November 2004. The membership was Alastair Campbell as chair (appointed in August 2004), Andrea Cook, Jayam Dalal, Baroness Finlay of Llandaff, Roger Higgs, Ian Hughes, Clara Mackay, Sheila McLean, Sally Smith, Sandy Thomas, and Christopher Wild (see Appendix A2 for members' biographies). They were appointed by an Independent Appointments Committee made up of Rev John Polkinghorne (Chair), Martin Bobrow, Niall Dickson, William Lowrance, and Geneva Richardson. It met on four occasions between November 2004 and August 2005 (<http://www.egcukbiobank/org.uk/index.html> 2005) (accessed 10/11/05).

The EGC was formed to serve as an 'independent guardian' of the EGF and to advise the BoD on its revision. It had an advisory capacity on the interests of participants and the general public regarding UK Biobank. The EGC would monitor the conformity of UK Biobank with the framework, reporting publicly on such conformity (<http://www.egcukbiobank/org.uk/index.html> 2005) (accessed 10/11/05).

### 3.7 Organisational Change (2004-2005)

The organisational structure of UK Biobank underwent significant changes in 2005, sparked partly by the resignation of John Newton as CEO of UK Biobank Limited on the 13 December 2004. Following his resignation, John Newton continued to represent UK Biobank at external meetings and events until March 2005. Tim Peakman was appointed acting CEO on the 17 January 2005, until a replacement was found (<http://www.ukbiobank.ac.uk> 2005) (accessed 10/11/05).

#### 3.7.1 Appointment of CEO *and* PI (2005)

Rory Collins was appointed CEO *and* PI of UK Biobank on the 8 August 2005, taking up the position formally on the 1 September 2005. Rory Collins was the Professor of Medicine and Epidemiology at the University of Oxford, a British Heart Foundation Professor and Co-director of the Clinical Trial Service Unit and the Epidemiological Studies Unit in Oxford. He continued in these roles and committed 60% of his time to his new position. He provided overall scientific leadership and as PI was responsible for finalising the protocol and implementing UK Biobank. The acting CEO, Tim Peakman, was appointed Executive Director also on the 8 August 2005 (<http://www.ukbiobank.ac.uk/news/pr/8aug05.php> 2005) (accessed 10/11/05).

#### 3.7.2 Organisational Changes (2005)

Following the appointment of Rory Collins the function of various groups and committees changed, the most significant being the function of the spokes. They were no longer responsible for recruitment and initial data and sample collection, which was to be managed centrally via the hub. Instead spokes were given the opportunity to compete for contracts to carry out various operational aspects, such as managing the call centre or training research nurses.

The Science Committee was disbanded and responsibility for developing the scientific protocol was given to a newly formed Implementation Group, composed of the six spoke leads and Rory Collins. It was this group, led by Rory Collins as CEO *and* PI, which had overall responsibility for delivering UK Biobank. According to the press



release issued on his appointment Rory Collins will 'lead and draw expert advice and support from a new Regional Investigators' Group comprising senior scientists from a series of Regional Collaborating Centres made up of groups of universities and medical schools' (<http://www.ukbiobank.ac.uk/news/pr/8aug05.php> 2005) (accessed 10/11/05).

### 3.8 Key Observations

I will now present key observations from this account of the chronology of UK Biobank. These observations are highly relevant in the origins and development of UK Biobank and are explored throughout the findings chapters.

UK Biobank's timing is in itself a source of controversy as it was marred by considerable delays. The original organisational structure was hampered by a series of delays in its development such as the appointment of the BoD, the Science Committee, the CEO, the hub and the spokes and the pilot studies, and most significantly recruitment. As we can see from the following table each of these milestones was delayed.

Table 4: Projected Targets and Actual Achievements<sup>66</sup>

	Projected	Actual
BoD established	Mid 2002	January 2004
Science Comm. established	Mid 2002	July 2003
CEO recruitment	Mid 2002	March 2003
Hub and Spoke selection	Mid 2002	March 2003
Pilot Studies	End 2002	February 2005
Recruitment	Mid 2003	February 2007

There was a certain amount of confusion surrounding the origins of the hub and spoke model, which is reflected in the sequence of events by which it was established. For example, the hub and spokes were appointed simultaneously, which added to the general confusion as the relationship between the two unfolded. The overall governing body, the BoD, was established long after the hub that it would lead. The hub and spoke model was a source of controversy throughout the origins and development of UK Biobank. The spokes' role in UK Biobank was never formally agreed and individual spoke membership was fluid. Unfortunately, there was no documentation in the material I analysed of any debate regarding the selection of the hub and spoke model. I am therefore unable to comment on who selected the model, why it was chosen and what alternatives were considered (see 7.3.2 for speculations

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<sup>66</sup>Projected targets are taken from the 2002 Draft Protocol 'Protocol for the UK Biobank A study of genes, environment and health'

regarding selection of the hub and spoke model). The model was however an early and integral part of the origins of UK Biobank and was cited in the initial protocol in 2001. The organisational changes exacerbated existing tensions between spoke members and representatives of the hub and funding bodies. A large number of academic scientists were involved in each of the six spokes and they included scientists of considerable stature. For example, the Scottish RCC included 19 senior academic scientists. Following two years of ongoing protocol development and contract negotiation, their original role ceased. The problematic nature of the original organisational structure is reflected in the fact that contracts between the hub and the spokes were never signed, participants were not recruited under that model, and organisational changes took place in 2005.

The proposal for UK Biobank was considerably developed after internal consideration within and between the funding bodies and consultation with the EWG, prior to the establishment of the PDC. The funding bodies undertook and commissioned numerous consultation exercises with the public and interest groups on ethical issues. The former leaders of the MRC and the Wellcome Trust and senior scientists within the funding bodies were strong advocates and their support for the resource was instrumental in its establishment. Their backing was secured before many of the academic scientists who would develop and implement UK Biobank were even aware of it. For example, the first official workshop between the MRC and the Wellcome Trust regarding what became UK Biobank took place in May 1999 and they agreed in principal to fund UK Biobank proposal in June 2000. On the other hand, the PDC was not established until May 2001 and the hub and spokes were not selected until March 2003. The funding bodies therefore sought to develop UK Biobank collaboratively only after having decided to fund it (albeit provisionally). Consultation undertaken with academic scientists in protocol development, for example, was limited by the fact that the funding bodies had decided to fund UK Biobank provisionally before the establishment of the PDC.

Leadership was a key issue in the difficulties of the original organisational structure as no individual was identifiable as a leader or scientific champion of the resource. Those individuals so prominent in the origins of UK Biobank who were responsible for getting it underway did not remain involved in the resource. For example, the then

leaders of the MRC and Wellcome Trust, Sir George Radda and Dr Mike Dexter and a senior scientist who led the EWG and the PDC, Tom Meade, were all near retirement when they became involved in UK Biobank and retired after the funding decision in 2002. As John Newton emerged as CEO around the same time that the hub, spokes and Science Committee were set up, his appointment was made amidst confusion regarding their respective roles. Furthermore because the hub's immediate authoritative body, the BoD, was not appointed until January 2004 John Newton did not have the support of an established infrastructure or funding bodies with which to lead UK Biobank.

## **Chapter 4**

**‘It’s not done in the normal way’ [025, p. 36; p. 4]**

### **Emergent Issues: ‘Standard Academic Scientific Practice’**

#### **4.1 Introduction**

Academic scientists, specifically previous and current committee members and spoke members, criticised the establishment of UK Biobank for departing from what I have termed ‘standard academic scientific practice’. Representatives of the funding bodies or UK Biobank Limited only referred to standard academic scientific practice when discussing the nature and process of the organisational changes in 2005. Academic scientists pointed to the following events and issues that demonstrated departure: protocol development, funding, development of the EGF, leadership, organisational structure, and the organisational changes. This chapter will address these events and issues in analysing portrayals of the establishment of UK Biobank as departing from standard academic scientific practice. I will present these events and issues chronologically. To recap briefly, following evaluation of the initial scientific protocol, the funding bodies decided to fund UK Biobank in March 2002. Once the funding decision was taken the protocol continued to be developed in tandem with the EGF, the CEO was appointed and the organisational structure was set up. The organisational structure was changed following the appointment of Rory Collins as CEO *and* PI in August 2005. In addressing these events and issues, I will examine the meanings attached to standard academic scientific practice and the perceived consequences of departure from it. First, I will explore academic scientists’ definitions of standard academic scientific practice.

#### *Definitions of Standard Academic Scientific Practice*

Members of the academic scientific community rarely explicitly defined standard academic scientific practice. This is surprising given the extent to which they referred to it. There was an assumption of a shared and singular understanding of the term, as if it did not need definition or explanation. However, it was clear that academic scientists were not referring to a single model, but rather a range of models. For

example, some described it as response-mode funding where scientists put forward proposals to funding bodies. These proposals are peer-reviewed and the funding body, usually a committee made up of scientific peers, decides whether to fund it. Others articulated standard academic scientific practice as scientists responding to a call for proposals on a specific area, selected by the funding bodies. ‘Commissioning’, whereby scientists would compete to carry out a research proposal designed by the funding bodies was also referred to as standard academic scientific practice.

Academic scientists more commonly articulated what standard academic scientific practice was not. In doing so, they defined it by its difference from a ‘business model’, which was also not explicitly articulated and was assumed to be a single model. Spoke members particularly adopted the term to distinguish the establishment of UK Biobank from standard academic scientific practice. They associated aspects of the establishment of UK Biobank with which they were not familiar, such as the setting up of the hub as a company (UK Biobank Limited) and the recruitment of a CEO with the business model. Spoke members identified themselves as the academic scientific community and the business community as representatives of UK Biobank Limited (the hub). The hub and spoke model was seen to therefore reflect a convergence of these different groups (academic scientists and business people) and was therefore a major issue in academic scientists’ perception of the establishment of UK Biobank as departing from standard academic scientific practice.

## 4.2 Protocol Development

**‘The protocol left unresolved a whole series of issues’ [070, p. 109; p. 10]**

Academic scientists criticised initial and ongoing protocol development for representing a departure from standard academic scientific practice. They criticised the initial protocol for its lack of detail and attributed its consequent ongoing development to key difficulties in the origins and development of UK Biobank, particularly time delays and decision making. For example, a member of the BoD stated: ‘the protocol left unresolved a whole series of issues, not least age range, the nature of information that was going to be asked from patients, the method of recruitment’ [070, p. 109; p. 10]. He commented on the resulting difficulties in reaching consensus: ‘All those questions were controversial ones which people can argue about until the cows come home and do argue about’ [070, p. 109; p. 10]. Some academic scientists felt that the protocol should have been decided prior to wide-scale consultation amongst the various committees. This perception is contrary to that of the funding bodies who decided that spoke members should be involved in ongoing protocol development.

### 4.2.1 The purpose of the protocol

Academic scientists contrasted the purpose of the initial protocol with standard academic scientific practice in that a complete protocol was not required for the funding decision. They felt that the initial protocol was developed to secure funding rather than, as in standard academic scientific practice, to detail how the resource would be delivered and on that basis secure funding. For example, a member of the BoD stated:

we ended up with a protocol which was a protocol to get the funding and wasn’t the science protocol that was actually going to be carried out and so we’ve spent the last year and a half writing the protocol for the study [070, p. 110; p. 11].

Academic scientists attributed this alleged deviation from standard academic scientific practice to the purportedly over-involved role of the funding bodies in UK Biobank, which they felt was unusual. They argued that traditionally scientists would be more involved than the funding bodies in developing the idea for an initiative. For

example, a spoke member said: ‘you have an idea, you apply for a grant, if they think it’s a good idea you get it whereas here the MRC and the Wellcome Trust decided they’re going to fund the project and they asked people to apply to take part in it’ [0502, p. 176; p. 3]. This is an articulation of standard academic scientific practice as response-mode funding. Academic scientists criticised the approach for representing the funding bodies’ commitment to the resource prior to that of the wider academic scientific community. For example, a member of the EWG remarked:

you also are in a slightly different sort of situation when the funding agencies have expressed an interest before anyone has come up with a protocol...it’s not that the funding agencies thought of it, epidemiologists partly thought of it but nevertheless they didn’t just come in and say here is a good idea and we want money, they just said do you think this is a good idea and then it became a much more interactive thing [061, p. 96; p. 5].

They also criticised the Biobank approach for not allowing as full an evaluation of the merits of the idea as there would have been if it had followed the standard approach of making the funding decision on the production of a complete protocol. For example a spoke member stated:

it seems a little, you know, back to front in as much as that what would normally happen with a scientific idea for a project would be that somebody puts together a protocol, it’s subjected to proper peer review and then on the basis of that it’s decided whether or not this project is a good idea for somebody with money to spend their money on. In a way what happened with Biobank was it was decided that it was a good idea and somebody was going to spend on it and then we had to develop a protocol [0105, p. 141; p. 6].

Similarly, a member of the PDC argued that committing funds in principle prior to the production of the initial protocol was detrimental to the process of protocol development:

it was probably lacking the sort of ambitious senior input that you would have got had we been applying for money but the money was already there on the table and we were just writing the protocol for something that was there [024, p. 32; p. 3].

However, some academic scientists defended the commitment of funds, in principle and actuality, prior to the development of a final protocol as indicative of standard



academic scientific practice, which reflects multiple understandings of the concept. They referred to the difficulty of setting up such a resource without the commitment of funds. For example a member of the EWG stated:

I think that's the way these things happen. I've been involved in discussions about the setting up of other big studies and to start off with you have to develop a proposal really and you haven't got the funds to set up a centre to actually do anything in practice and that's what the proposal is all about. It's to get the funds going for all that to happen. So I don't think there's anything surprising about that [060, p. 92; p. 3].

#### 4.2.2 Consultation undertaken in protocol development

Academic scientists criticised the consultation undertaken with the academic scientific community, in initial protocol development prior to the funding decision, and ongoing protocol development following the funding decision, as departing from standard academic scientific practice. It is interesting to compare the opinions of academic scientists involved in initial protocol development (PDC members) with those involved in ongoing protocol development (spoke members) on the consultation undertaken in protocol development.

Regarding initial protocol development prior to the funding decision, members of the PDC felt that key decisions, such as sample size and age range, were decided prior to their establishment. They contrasted this with perceived standard academic scientific practice where a group like theirs would form and design the entire protocol independently without direction. For example, a member of the PDC commented on the didactic nature of the consultation with the Committee: 'we were told "you will design a protocol. This is the study. It must be half a million. It must address A, B and C" so it was almost a study written by the chief executive' [024, p. 32; p. 3]. They presented the 'normal' way in which protocols are developed as an intrinsic feature of the academic scientific community. Again, we see the perception that a single model of standard academic scientific practice exists where protocols are developed independently by the scientific community. For example, 024 continued:

That's a very unusual way of doing things. We are normally used to the situation where a group of scientists would come together and come with the

protocol, the suggestions and apply for the money. This was sort of the reverse, so it was difficult. When it eventually went to international reviewers there wasn't a uniform agreement that all the things were right and this is because it was driven and organised in a slightly strange, unusual for the scientific community, fashion [024, p. 32; p. 3].

Members of the PDC implicated senior figures in the funding bodies in making key protocol decisions prior to any consultation. For example, a member of the scientific community outwith UK Biobank stated: 'it's been set up and managed along the lines of something where the decision to do a study has been taken from above as it were and then it was fulfilling the requirements that had basically been decided' [0700, p. 189; p. 2].

The minutes of the PDC meetings reflect the extent to which certain issues were up for debate, the difficulties faced by the committee in reaching consensus and the resulting tensions. One such issue was sample size. There was a view in the PDC that senior representatives of the funding bodies decided on the sample size prior to consultation with the Committee. For example, in the minutes of the third meeting a query regarding the merits of 'fixing the sample size at this stage' received the reply that 'a great deal of work had gone in to the earlier estimates of sample size with an expert group led by Nick Day' [D550/33 Volume 2]. The PDC was aware even earlier of the perception that the protocol was agreed prior to their establishment and expressed unease accordingly. This unease is evident in the minutes of the second meeting of the committee. Members voiced concern that the draft report of the Protocol Development Workshop [a consultation exercise undertaken with the wider academic scientific community] 'gave the impression that outcomes were definite decisions instead of recommendations'. It was agreed that the preface to the report should

emphasise that nothing within the recommendations arising from the workshop was proscriptive and the responsibility for deciding which recommendations could and should be implemented rested with the Protocol Development Committee [S600/174 Volume 1].

The tension resulting from the perception that key aspects of the protocol were decided prior to the establishment of the PDC is evident, and members of the Committee consequently challenged the validity of the consultation undertaken with

them. For example, on 16 November 2001 (prior to the fifth and final meeting of the PDC) a PDC member wrote a letter recommending the inclusion of the following paragraph in the covering letter to the international peer review panel: '[t]he PDC has worked under firm guidelines from the funders that the framework should be based on an achieved sample of about 500,000 middle-aged adults all of whom are assessed in a similar manner' [S600/174 Volume 1].

The initial protocol continued to be developed following the disbandment of the PDC, the funding decision and hub and spoke selection. Spoke members criticised ongoing protocol development for departing from standard academic scientific practice for different reasons. On the one hand, spoke members criticised ongoing protocol development, feeling that the protocol should have been agreed prior to their selection. On the other, they criticised ongoing development because of the perceived lack of consultation with them in developing a protocol that they would be responsible for implementing. They described feeling a lack of identity with the protocol as a result of insufficient consultation, for example, a spoke member said:

it seemed to have been done remotely and distantly from the scientific community. It's been done somewhere centrally by a committee and I suppose that is necessary because somebody has to take forward the agenda but I don't have a strong sense of identity with the scientific protocol [0104, p. 139; p. 4].

This criticism of a lack of involvement and connection with the protocol reflects tensions between the hub and the spokes. For example 0104 continued:

normally in developing a protocol you would do that in conjunction with your research team and there's not that sense, I mean there's a sense at the lowest level, which, you know, the RCCs are really just data collection houses rather than people who are in their own right senior researchers who are able to give specific advice to the project and I'm not sure that's been fully capitalised on [0104, p. 139; p. 4].

The first group argued that standard academic scientific practice dictates that the protocol would be finalised prior to spoke selection and therefore spoke members would not be involved in its development. The latter group argued that standard academic scientific practice dictates that those responsible for implementing the protocol would be intimately involved in developing it. Spoke members referred to standard academic scientific practice as a single model yet they articulated it in

opposing ways. This mirrors different articulations of the commitment of funds prior to final protocol development as representing both adherence to and departure from standard academic scientific practice.

### 4.3 Funding

**‘People saw it as a cuckoo in a nest competing with this supply of money for their bread and butter projects’ [010, p. 1; p. 2]**

The central paradigm of standard academic scientific practice as ‘good practice’ is evident in academic scientists’ criticisms of the funding of UK Biobank, the calculation of the funding figure and the role of the funding bodies as being contrary to standard academic scientific practice.

#### 4.3.1 The funding of UK Biobank

Academic scientists and some representatives of UK Biobank Limited felt that funding UK Biobank at all was contrary to standard academic scientific practice because of its nature. They distinguished UK Biobank-type initiatives from more traditional research activities on account of their long-term, prospective nature, scale and potential to address a range of conditions. Academic scientists and some representatives of UK Biobank Limited articulated standard research as short-term, supported by a single institution, focussed on a single condition and designed with a specific hypothesis in mind. For example, a member of UK Biobank Limited commented:

it’s always very difficult to get funding for infrastructure projects...whereas if you put together a small project which has a three-year cycle to it and a research paper at the end of it, everybody can understand it and it gets funded, so I think there’s a cycle of funding [010, p. 1; p. 2].

They associated the nature and convergence of the funding bodies involved in UK Biobank, in terms of their scale and prestige, as a departure from standard academic scientific practice. For example, the member of UK Biobank Limited contrasted the funding of UK Biobank with the usual pattern of research funding in the UK:

research funding in the UK has painted itself into a corner, which is a relatively small number of universities doing a lot of work on a small number of problems and they get a lot of the funding and what Biobank has done is to produce a resource which is of very high quality and is funded by the blue chip funders and yet is able to address any common disease [010, p. 1; p. 2].

Representatives of UK Biobank Limited and some current committee members attributed academic scientists' criticism of UK Biobank to the fact that it represented the type of research not traditionally funded and fears that it would negatively affect the funding of other research. For example, 010 continued: 'people saw it as a cuckoo in a nest competing with this supply of money for their bread and butter projects and in fact it was a misapprehension' [010, p. 1; p. 2]. They attributed hostility toward UK Biobank to such lack of familiarity with UK Biobank-type initiatives. For example, a member of the BoD remarked: 'these big genetic epidemiology studies are a little bit out of the mainstream biomedical sciences, some of the mainstream scientists probably would have looked on it with a bit of suspicion' [013, p. 15; p. 1].

#### 4.3.2 Calculation of the funding figure

All constituent groups of interviewees debated the purpose of the initial funding figure. Some academic scientists criticised it and thought it was inadequate because it did not include the complete costs for UK Biobank, including follow-up of participants and the costs of genotyping every sample. Other academic scientists defended the initial funding figure arguing that it should not project the entire costings for the resource over its existence, but should just estimate the costs of setting up the resource. Hence, the calculation of an accurate and complete figure was not as important. Proponents of the latter argument acknowledged the inadequacy of the funding figure in covering all costs associated with the resource in the long-term, but stressed that future funding would meet such costs. For example a member of the BoD remarked:

the point in which to argue that is when the whole study is successfully underway, when we are beginning to see some early results and I think there will be a moment when a lot of the other big funders of science and medicine projects will come behind this. I don't think we could ask any more of the funders than the contributions made at the moment...now is not the time to ask for more, the time to ask for more is when the project is in full swing [013, p. 16; p. 5].

Similarly, a member of the EWG defended the funding figure by reflecting on its purpose:

It's a perfectly adequate amount of money to see whether it is possible to set up and run this study. It is clearly not an adequate amount of money to follow that group of people for 25 or 30 years and do all the genotyping. It was never intended to do so [061, p. 98; p. 9].

Each argument was supported by reference to standard academic scientific practice. Academic scientists criticised the funding figure for departing from standard academic scientific practice as it did not include the complete costs for the resource. Others defended the funding figure for adhering to standard academic scientific practice because it did not include the complete costs for the resource. For example, the member of the EWG commented: 'That is a standard model for funding any very long-term programme. Only a fool would make a commitment to funding it for the next 30 years, just not sensible' [061, p. 98; p. 10]. This analysis illustrates confusion over the nature of standard academic scientific practice as the calculation of the funding figure is felt to represent both adherence to and departure from it for the same reason.

A key part of this debate that further polarised opinion amongst academic scientists was the extent to which an accurate initial funding figure *could* be calculated. Some academic scientists who defended the funding figure argued that it was not possible to calculate the complete costs of UK Biobank. For example, a member of the Science Committee stated: 'nobody knows what the budget of this is going to be because we won't know until we do the pilots' [012, p.13; p. 5]. Those critical of the figure argued it was not only possible but of utmost importance to calculate the complete costs of UK Biobank and they viewed the failure to do so with suspicion. For example, a member of the PDC argued that:

They could have done a much better job with the overall costs but they should have been honest and upfront about the genotyping costs and if they had it would have been very clearly well over a hundred million, probably several hundreds of millions to complete this project [051, p. 84; p. 14].

#### 4.3.3 Role of the funding bodies

Academic scientists expressed concern that the funding bodies were taking too active a role in UK Biobank. For example a spoke member remarked: 'It's a bit shady

because their names are there as observers but they're clearly not' [025, p. 34; p. 5]. They contrasted their role in UK Biobank with that traditionally undertaken by funding bodies in research activities. Academic scientists argued that by adopting a more involved position than usual the funding bodies, as opposed to the scientists, were in control of UK Biobank. They contrasted this with standard academic scientific practice where the scientists, particularly a PI, would be in control and viewed this alleged departure with suspicion. For example 025 continued:

In normal studies the funders make an agreement to give a grant and then they leave the project to the scientific investigator who is then charged with the responsibility of delivering upon it...the funders are clearly far, far, far more involved than any other study of its kind and not always up front either [025, p. 35; p. 5].

Academic scientists accused the funding bodies of creating confusion about ownership of UK Biobank by being so involved. For example a spoke member reflected:

It is a strange set up as usually funding takes two forms: the idea is approved and people are given the money to do it or (mostly in the private sector) funders give people the money to manage the project but it is still their project. UK Biobank is trying to do both. It invited investigators to take part but the funders have not allowed them the authority to take care of the science [030, p. 42; p. 3].

This quotation also illustrates the different articulations of standard academic scientific practice. Usually academic scientists defined it as a single model whereas here the interviewee defined it in two ways, as response-mode funding and commissioning.

Some academic scientists justified the unusual role of the funding bodies because of the nature of UK Biobank itself which, given its scale, profile and sensitivities surrounding the field was felt to deviate from standard research activity. They argued that the role undertaken by the funding bodies mirrored the unusual nature of the resource. For example, a spoke member commented:

there was a slight amount of nervousness from the stakeholders about the public perception of this project... [they were] quite concerned about not being tarnished in any way by being associated with a project that was going



to be a major barrier or stir up a lot of concerns about ethics [080, p. 121; p. 8].

Academic scientists further justified the role undertaken by the funding bodies on account of their stature and responsibilities. For example, the size of the financial investment was felt to warrant such a role, as a member of the EWG stated: 'If you take a single investment the risk of failure is too high to have it anything other than under close management scrutiny' [062, p. 102; p. 7]. They further stressed the funders' social and scientific responsibilities as an explanation for their role. For example, a member of the BoD remarked: 'they've got to be accountable...the funders have a responsibility to taxpayers, to their trustees, to politicians and to the public generally' [070, p. 108; p. 9] and a spoke member commented on: 'the need to defend what they're doing against the possible moans or complaints from researchers who can't get money from them for other projects' [0200, p. 145; p. 4].

#### 4.4 Development of EGF

**‘It’s good that they were trying to sort of tackle all these elements together rather than just sort of tagging on the law, ethics and social bit at the end, which so often happens’ [091, p. 127; p. 2]**

The central paradigm of standard academic scientific practice as ‘good practice’ was complicated by perceptions of the development of the EGF. Members of the IAG and the EGC praised the development of the EGF in tandem with the initial scientific protocol for departing from standard academic scientific practice.

##### 4.4.1 Support for EGF development in tandem with protocol development

Members of the IAG and EGC welcomed the development of the EGF in tandem with the protocol as demonstrating the appropriate message to the public and commitment to ethical, legal and social issues. They felt that it showed the public that ethical, legal and social issues were as significant as scientific issues. For example, a member of the IAG stated: ‘in terms of the impression that the funders are giving to the public and to others it’s very important to say “We are open and responsive to suggestions as to how we can best set up this framework”’ [091, p. 127; p. 2]. IAG and EGC members presented the establishment of UK Biobank as departing from standard academic scientific practice whereby ethical, legal and social issues would be considered following the resolution of scientific issues. For example 091 said: ‘it’s good that they were trying to sort of tackle all these elements together rather than just sort of tagging on the law, ethics and social bit at the end, which so often happens’ [091, p. 127; p. 2]. They criticised standard academic scientific practice as demonstrating a lesser commitment to ethical, legal and social issues than to scientific ones. For example, a member of the EGC praised the approach adopted because it:

accords the ethical and legal stuff a level of importance in the organisation that you don’t always see...they usually tack it on at the end whereas this has been as carefully thought out as the scientific stuff which I think is actually quite unusual [0400, p. 167; p. 6].

Members of the IAG and EGC further criticised standard academic scientific practice with reference to the consideration of ethical, legal and social issues in the HGP,

which was presented as representative of the standard approach. Interviewee 0400 went on to contrast the approaches:

it's not all that common for big ventures of this sort to take ethical, legal governance quite so seriously...although with the human genome project for example the Americans put all this money into ethical, social and legal issues but in fact it was 3% of their budget and it really didn't produce anything very interesting because it was just commissioned research from various people [0400, p. 166; p. 7].

#### 4.4.2 Difficulties of EGF development in tandem with protocol development

IAG and EGC members did however acknowledge the difficulties of developing the EGF in tandem with the scientific protocol, especially to a protocol that was itself evolving. For example, a member of the IAG stated:

one of the biggest problems was not being completely clear about the scientific basis for the project before they started looking to pull in other areas of expertise such as legal, social and ethical and looking at the practicalities [091, p. 127; p. 1].

They felt that the problematic nature of protocol development contributed to the difficulties of the approach, for example the interviewee continued:

the main driver was the science and because the science committee kept revisiting issues and there was lots of outside input and criticism that kept being revisited, which then had a necessary impact on the other areas and that therefore became quite difficult to coordinate [091, p. 127; p. 2].

Members of the IAG and EGC attributed the shortcomings of the EGF, namely its lack of detail on particular issues, to it being developed in tandem with the scientific protocol. A member of the IAG reflected on this:

That's why the framework doesn't give much advice on such things as the IT system or on anonymisation of data or things like that because we simply didn't know what might be considered from a technical point of view [090, p. 123; p. 13].

Members of the IAG reflected upon how they foresaw the difficulties associated with developing an ethical response to a changing scientific protocol and took steps to

address them. For example, they invited representatives from the funding bodies and the Science Committee to attend their meetings. This demonstrates the importance given to communication between the groups in developing their respective documents (the EGF and the protocol), given their evolving nature. IAG members stressed the significance of representation from the funding bodies and the Science Committee in informing their deliberations. They also stressed how they had invited such representation to their meetings rather than it being imposed upon them. For example a member of the IAG stated:

we ourselves invited the funders to send representatives to our meeting. They had initially said “We think this ought to be independent” we said “we are grown-ups and we will maintain our independence, don’t worry about that but we don’t believe we can operate in a vacuum because you the funders are barging ahead setting up Biobank you know an awful lot more about it that we just simply don’t know” [090, p. 123; p. 8].

Members of the IAG did however acknowledge the difficulties of this interaction between them and representatives of Science Committee. They presented the difficulties as resulting from the differences between the IAG and the Science Committee in terms of academic discipline, which were exacerbated by the evolving nature of the protocol. For example, another member of the IAG remarked:

I certainly felt that the science committee was this sort of amorphous body “over there” and the occasional person would come in and talk to us about it and we could ask him all the questions we wanted but it still kind of felt we don’t really know what is going on over there [091, p. 127; p. 14].

Despite the difficulties associated with the development of the EGF in tandem with the scientific protocol, support for the strategy was maintained. IAG members related the difficulties to the fact that the approach was novel rather than any intrinsic flaws with it. They stressed the need to refine the approach to address these difficulties, given the benefits associated with it. For example, a member of the IAG reflected:

I wholly approve of trying to deal with all these elements at the same time, I think for future lessons more thought is required as to how does one actually time these issues because we said on numerous occasions “Well from what you’re telling us just now this is what we recommend but if this changes, well, then our recommendations might change” [091, p. 127; p. 8].

Interestingly, some members of the IAG downplayed the difficulties associated with the approach by minimising the extent to which it did depart from standard academic scientific practice, which represents an attempt to divert criticism of the approach. Hence we see a return to the familiar central paradigm of standard academic scientific practice as ‘good practice’. For example, a member of the IAG remarked:

some people thought that the interim advisory group was set up far too early, we should have been established much later when the science was clear and the board had worked and all that. Other people said “Too bad this group’s been set up too late because these ethics issues and so on need to get sorted out before the science committee gets started”. We just said “Look this is not unusual in a start-up, we are where we are, we think we can do some good, so we will advise and we will develop the framework and will propose a framework to the funders”. You often in advising have to deal with uncertainties and we did [090, p. 124; p. 13].

Although academic scientists not directly involved in the consideration of ethical, legal and social issues and representatives of UK Biobank Limited commented less on the development of the EGF in tandem with the protocol they criticised the approach. They felt that addressing the ethical, legal and social issues at the time they did delayed the development of UK Biobank generally, particularly the completion of the protocol and the establishment of the organisational structure. For example, a member of UK Biobank Limited remarked: ‘essentially what they did was to stop all work on the science and do the ethics and governance framework and that distracted them and I’m sure that was seen as the major thing to get done’ [010, p. 4; p. 13].

## 4.5 Leadership

**‘Every other study always has a principal investigator or a team of principal investigators who are responsible for everything from the budget to design. Here it’s not even clear who is responsible for anything’ [025, p. 37; p. 5]**

Academic scientists criticised the leadership of UK Biobank, particularly the lack of a PI as contrary to standard academic scientific practice. Similar to their criticism of the role of the funding bodies, some academic scientists sought to rationalise the approach taken whilst underlining their disapproval.

### 4.5.1 Lack of a PI

Spoke members and current committee members in particular connected the lack of a leader equivalent to a PI with the lack of a single decision-maker responsible for taking UK Biobank forward. For example, a spoke member remarked:

Every other study always has a Principal Investigator or a team of Principal Investigators who are responsible for everything from the budget to design. Here it’s not even clear who is responsible for anything. You might think the Science Committee is responsible for the science but you can’t actually do the science without the budget so if the budget’s held at the BoD then naturally you’ve got a mismatch, you’ve got a problem [025, p. 37; p. 5].

They associated the organisational structure of Biobank, specifically the hub and spoke model, with this perceived lack of leadership. For example, a spoke member commented: ‘it’s not done in the normal way where we have either one or a few senior leaders who are wholly responsible’ [025, p. 36; p. 4]. Similarly, a member of the Science Committee stated:

most of these studies are run by one group they just get on and run the study...this is being run by six groups plus a hub and it makes it much more difficult to manage...the other way to do it would have been to say “right, we’re going to give this guy X amount of money to do the study and let him get on with it” [012 p. 13; p. 8]

He defended this departure from the norm because he felt that UK Biobank itself departed from standard research in terms of its scale, but stressed the difficulties caused by this approach, specifically of such wide-scale consultation: ‘they needed

this to be seen as a truly national programme. I mean there's a good reason for it to be but it's just if you're going to do it without all the peripheral issues, you just choose one guy and say 'get on and do it'' [012, p. 14; p. 8].

Spoke members criticised the hub and spoke model for representing a convergence of the academic scientific community and business community in contrast to standard academic scientific practice. They described the PI as an intrinsic feature of the academic scientific model as opposed to the business model. Hence, spoke members argued that the lack of a PI was a denial of the practices of the academic scientific community in favour of the business community. For example, a spoke member stated:

in the scientific community we are used to studies where there is a chief investigator or if there is a multi-centre study a chief investigator and principal investigators who sign up to a collaboration and a shared ideas approach and this is slightly, well extremely different [0201, p. 146; p. 3].

This reflects the tensions between the hub and the spokes in the difficult and ultimately unsuccessful process of contract negotiation.

#### 4.5.2 Lack of a figurehead

Academic scientists, particularly previous committee members, criticised the organisational structure for representing a departure from standard academic scientific practice on account of the lack of an identifiable figure with the passion to deliver UK Biobank. They presented the HGP as illustrative of standard academic scientific practice in that there was a recognisable leader intrinsically connected with the endeavour. For example, a member of the EWG remarked:

it's very atypical...if you go back to your human genome analogy there's no question who was identifiable for the UK, if it's the human genome project it's John Sulston, you don't stop and think about it, it's blindingly obvious and you can't do that here and it's unusual [061, p. 96; p. 7].

Academic scientists associated high-profile leadership with the passion, personal commitment and effort required to drive initiatives forward. For example, a member of the IAG stated:

Biobank has not had the kind of Nobel laureate, high-level support that the Genome Project did...[that] succeeded to my mind, in part because some very well-placed people at the prime of their careers said ‘The time has come, let’s do it’ and they put their shoulders to it and made it happen and they were willing to take public stances, give speeches, meet with the US Congress and beg for money, go before the Parliament, defend it before the Medical Research Council, those kinds of things ... They fought for the Human Genome Project, they also served as diplomats to get the Japanese and others involved and they made it happen and then they crunched along and finished ahead of time and below budget and it takes stars to make that happen...it (Biobank) hasn’t had the same kind of public face that the human genome project did, a stream of articles in a science magazine [090, p. 126; p. 4].

#### 4.5.3 Explanations for the perceived lack of leadership

Academic scientists contrasted the way in which the idea for UK Biobank developed through the funding bodies and various workshops and groups (for example, the Joint MRC/Wellcome Workshop and the EWG) with the perceived standard way in which ideas develop from an individual. They therefore attributed the departure from standard academic scientific practice represented by the lack of leadership to the origins of UK Biobank. For example, a member of the EWG contrasted the origins of UK Biobank with the standard way in which ideas develop: ‘Mostly the way science is funded is someone has an idea that they wish to pursue and they go out and drive it and find the money to do it and that hasn’t gone that way’ [061, p. 97; p. 7]. This interviewee defined standard academic scientific practice as response-mode funding, which he associated with strong leadership.



## 4.6 Organisational Structure

**‘It’s a very odd sequence...they got the cart before the horse’ [070, p. 109; p. 5]**

Academic scientists, particularly spoke members, criticised the organisational structure of UK Biobank, in particular UK Biobank Limited, the selection and establishment of the spokes, the establishment of committees and the sequence of establishment as departing from standard academic scientific practice. These criticisms echoed those concerning the perceived lack of leadership. For example, academic scientists stressed how unfamiliar they were with the establishment of the hub as a charitable company, UK Biobank Limited.

### 4.6.1 Establishment of UK Biobank Limited

Academic scientists criticised the establishment of the hub as a charitable company, UK Biobank Limited, rather than just as a central organisational body, because it represented a departure from standard academic scientific practice. Their criticisms chiefly concerned the convergence of the academic scientific community in the spokes and the business community of the hub.

Academic scientists identified the establishment of the company with the practices of the business community and as a process not familiar to academic scientists. The business model was not clearly defined; rather it was presented as a model in opposition to that of academic scientists. For example, a member of the PDC remarked: ‘this was completely alien to the majority of the people in the audience, the idea that you set up a company to run a study’ [051, p. 86; p. 5]. Some academic scientists tried to understand the rationale for establishing UK Biobank Limited. They acknowledged the need for an organisational structure that reflected the involvement of multiple, powerful funding bodies but felt that UK Biobank Limited was too much of a departure from standard academic scientific practice. The PDC member continued:

there may be good reasons for having something unusual for an institute that’s funded by three major agencies...but you don’t have to have, you know, a public limited company running the show, you don’t have to have competitive tendering in what is in a sense the worst of the business environments. You

don't have to have a chief executive function which was sort of more or less invented...the whole thing was invented by people who knew nothing about the way in which the scientific community works [051, p. 85; p. 11].

This quotation illustrates the academic scientists' differentiations between the academic scientific community and business community in terms of personnel. The interviewee distinguished between academic scientists and business people who 'knew nothing about the way in which the scientific community works' [051, p. 85; p. 11].

Much of academic scientists' criticism of the organisational structure concerned the perceived power it granted to the business community in the hub over the academic community in the spokes. Spoke members in particular criticised this balance of power as departing from standard academic scientific practice whereby the academic scientific community would be in control. This tension between the academic scientific community in the spokes and the business community in the hub is evident in the documents relating to contract negotiation between the hub and the spokes. The key source of tension was the policy that spokes would not be granted any early or preferential access to the data or samples, which spoke members criticised for departing from standard academic scientific practice. Spoke access to the resource was a major issue in the origins and development of UK Biobank (addressed fully in chapter six). Spoke members presented this issue as illustrative of the difference between the two research communities and the tone of contract negotiations reflects this perceived gulf in practice. For example, in response to the draft contract on the 30 April 2004 a spoke member commented:

[i]t is quite usual for this intellectual input (through the involvement of senior expert researchers) to be provided to joint projects essentially without cost. This is because the pay-back is through (1) overheads recovered, (2) academic outputs (publications etc), (3) spin off projects and (4) the prestige and consequential benefits that arise from association with a quality project. Unfortunately at present colleagues from many of the RCCs I have spoken to have failed to see how this contract will provide any of these, let alone all of them [D550/10 Volume 1; p. 43].

Spoke members further distinguished the academic scientific community from the business community with reference to the public and private sectors inhabited by

each. They criticised UK Biobank Limited for occupying both sectors and as such representing a departure from standard academic scientific practice. A spoke member however acknowledged the extent to which such an approach was increasingly common in the public sector:

it's very, well weird isn't exactly right but it's unusual for me. It's a very New Labour, Third Way of doing things, it's like a semi-public thing when you set-up a company to run it...it's a sort of political fashion, I don't know, I think some people in Government believe that bureaucracies work if they're based on privatised models and it's a sort of semi-privatised model [052, p. 89; p. 6].

This convergence of the academic scientific and business community, and the public and private sector associated with the establishment of UK Biobank Limited, is also evident in the documents relating to hub selection. This material reflects understandings of the different values connected with each community. The bidders for the hub contract were judged on wide ranging criteria including their business and academic case. For example, the S.W.O.T. (Strengths Weaknesses Opportunities Threats) analysis reports for each of the bidders for the hub contract dated the 11 of February 2003 state 'lack of entrepreneurial vision' or 'no entrepreneurial feel' as weaknesses [D550/12 Volume 1; p. 35]. The Host Selection Site Visit Report Conclusions dated the 6 March 2003 imply unease regarding overt academic strength. For example, comments included: 'there was an impression that overwhelming academic influence could easily overpower the Hub's autonomy' [D550/12 Volume 1; p. 35].

#### 4.6.2 Spoke selection and establishment

Spoke members criticised the hub and spoke bidding process and their subsequent establishment as contrary to standard academic scientific practice.

Spoke members criticised the bidding process because of the confusion regarding the nature of the contract for which they were bidding. They criticised this lack of clarity as contrary to standard academic scientific practice. For example a spoke member recalled: 'it was a bit mysterious really... it was strange because we were kind of not bidding for actual money or anything, we were kind of bidding to be part of

something but we didn't actually know what' [0203, p. 153; p. 9]. He contrasted this situation with the perceived standard approach: 'normally you would submit an application for a commissioned piece of research, you knew how much money you were going to get and roughly what, you know, the slot was and what the topic was and then you would be told 'yes, you've got a certain amount'' [0203, p. 153; p. 9]. The interviewee articulated standard academic scientific practice as a single model in which scientists apply to carry out a research project designed by the funding bodies in full knowledge of the costs and timescales required. He contrasted this with UK Biobank because of the fact that applicants were not informed of the design, costs and timescales involved.

Spoke members also described the process that followed the bidding process as deviating from standard academic scientific practice. They criticised the lack of progress, in terms of research activity and release of funding, following selection. Spoke members contrasted the outcome of the bidding process for UK Biobank with the outcome of other competitions that they implied represented standard academic scientific practice. For example a spoke member reflected:

normally after that process had gone through and you'd been told either 'no, your tender has not been successful' or 'yes, it has been successful' then it would be a case of 'so go away and do what you said you were going to do' but what's happened with Biobank since then is that we seem to have been constantly revisiting the detail of exactly what the different spoke organisations are going to do, how is it they're going to do it and how much money they're going to have to do it [0105, p. 142; p. 7].

They were surprised at the lack of funding following a successful result. Spoke members felt it was odd that they were not given what they felt they had bid for. For example, one spoke member remarked:

normally when you apply for funds and you are granted your application you expect to get them ... 'It was completely the other way round "bid for the main project but we're not going to give you any money and we're going to ask you to do some pilots", madness! [0800, p. 193; p. 6].

Spoke members also criticised the timing of the pilot studies, (which were conducted following the selection of the spokes) as departing from standard academic scientific practice. This criticism relates to the confusion over the role of the spokes in UK

Biobank. Some spoke members felt that the pilot studies should have been carried out and evaluated, and their role should have been fully developed prior to their appointment.

The issue of the timing of the hub and spoke bidding process and their subsequent establishment was evident in the documents relating to spoke selection and protocol development. There was debate regarding the merits of appointing the spokes at a time that would allow them to contribute to protocol development. Representatives of the funding bodies were eager to include the spokes in protocol development, whereas some spoke members criticised the failure to finalise the protocol prior to their appointment. For example, representatives of the funding bodies partly justified their decision not to fund the IPC alongside the main protocol on the grounds that it was important to gain input from the spokes. The minutes from the final meeting of the IPC subgroup on 7 August 2001 refer to the position of the funding bodies on the issue: ‘it was agreed that the additional components needed to be added once expressions of interest had been made by the potential spoke organisations’ [S600/174 Volume 3; p. 16]. This therefore delayed aspects of development until the spokes were established.

Representatives of the funding bodies justified the decision to delay protocol development until the spokes were selected because of the perceived importance of their involvement in the protocol and resource generally. They felt that the potential for involvement in the development of the protocol was an important issue in attracting bids for the spoke contracts. For example, an e-mail between senior representatives of the funding bodies warned that further development of the protocol, deemed necessary for the funding decision, would negatively affect spoke participation in the resource and result in ‘lack of input of spokes to protocol development giving little ownership of the project and therefore little incentive to participate’ [S600/161 Volume 3; p. 27]. Members of the PDC were reluctant to postpone further development of the protocol to allow for spoke involvement and questioned the merits of spoke involvement. The difficulties of garnering the involvement of the spokes in protocol development were addressed by a member of the PDC: ‘if issues were left to the spokes it would be difficult to co-ordinate afterwards’ [S600/174 Volume 3; p. 16].

#### 4.6.3 Establishment of committees

Members of previous and current committees criticised the way in which committees were established as departing from standard academic scientific practice. They particularly criticised the establishment of temporary predecessor groups (the Project Board, the PDC and the IAG) to the permanent groups (the BoD, the Science Committee and the EGC). They saw predecessor groups as performing the same function as the permanent groups and did not regard them as separate entities with different purposes. For example, a member of the EGC reflected upon the disbanding of the IAG and the formation of the EGC in such terms: 'I think it must have been quite hard for them to be the start-up group and hand over to another group and that's an unusual model. Usually the groups that start something off pick them up and carry on with them' [0401, p. 170; p. 4].

Current and former committee members and some representatives of UK Biobank Limited doubted the value of replacing committees with newly established groups and felt that doing so hindered the development of UK Biobank. For example, the BoD could not be established until the company, UK Biobank Limited, was set up and its predecessor group, the Project Board, was disbanded prior to the establishment of UK Biobank Limited. A representative of UK Biobank Limited commented:

the Board were going to take over from the Project Board but the company wasn't set up until December 2003...all the really big decisions had to be made by the Board and of course the Board were completely new [010, p. 4; p. 14].

The interviewee described the replacement of temporary committees (Project Board, PDC and IAG) with permanent committees (BoD, Science Committee and EGC) as a pattern in the set up of UK Biobank. He attributed the time taken to establish the resource, which was described as lengthy, to this approach. For example:

people have been working away on the project and then they've just been stood down and then there's been a gap and then they bring in a new group and of course what happens is the new group takes a while to gel, to understand the project, to take it apart put it back together and then they start to be functional but it's a big delay in doing that [010, p. 4; p. 15].

His speculation regarding the rationale for such an approach reflected a wider theme regarding the funding bodies' efforts to involve the academic scientific community and avert criticism of a lack of consultation. Academic scientists however questioned the extent to which the funding bodies sought genuine consultation and involvement. For example, the same interviewee distinguished between wanting to be inclusive and wanting to be perceived as inclusive:

it's in an effort to be completely fair and to some extent not, they're obviously very keen that Biobank isn't seen as one person's pet project...but I think that one has to accept that this approach is debilitating and needs to die [010, p. 4; p. 15].

#### 4.6.4 Sequence of the establishment of UK Biobank

Academic scientists criticised the sequence in which the organisational structure was established, namely the appointment of the CEO and the set up of UK Biobank Limited prior to the establishment of the BoD, as contrasting with standard academic scientific practice.

Academic scientists discussed the effect of this sequence on control of the resource, protocol development and funding. They held the sequence responsible for difficulties surrounding control and decision making. The CEO was appointed at the same time as the hub and spokes were appointed, which made it difficult for him to assert his authority over the hub and UK Biobank generally. The ultimate authoritative body, the BoD, was the last to be established. This sequence meant that funds were not released until the BoD were appointed, which academic scientists contrasted with standard academic scientific practice where funds would be released prior to the establishment of the organisational structure. They also criticised ongoing protocol development following the appointment of the spokes and the science committee for resulting in the difficulties surrounding decision making and time delays. For example a member of the BoD described the sequence:

What happened was extraordinary, the other way around...what they had done is appointed a Chief Executive, with no Board to be accountable to and they'd appointed the RCCs on the basis that that was the model they were going to follow without having a protocol or having appointed the people who were

going to have to carry it through, and then they appointed a Science Committee which included people from the RCCs and they started writing the main protocol, and then they appointed the Board and gave the Board the authority to spend the money. So it's a very odd sequence...they got the cart before the horse [070, p. 109; p. 5].

Some academic scientists defended the timing of the appointment of the BoD on account of the nature of UK Biobank itself. They justified the sequence as a departure from standard academic scientific practice arguing that UK Biobank was itself a departure from standard research activity, on account of the involvement of multiple, powerful funding bodies and the scale of the financial commitment. For example, the member of the BoD stressed the need to secure funding prior to the appointment of committees: 'I can see why they did it, it was in order to sign off the funding, which was the key decision that drove everything, you can't have the Board set up before the funding' [070, p. 109; p. 5].

As discussed in the previous sub-section, academic scientists also criticised the timing of hub and spoke selection in relation to protocol development. They held ongoing protocol development as responsible for the difficulties over leadership of UK Biobank. This criticism relates to the difficulties of reaching consensus amongst a large number of scientists both in the science committee and in the spokes, and the merits of such consultation in developing the protocol. A clinical academic involved in UK Biobank argued that the protocol should have been developed and finalised by a previously appointed leader as opposed to ongoing protocol development with a wider franchise: 'decide what you want to do and advertise applications, decide who was going to actually lead it and do it and then get *them* actually to write the detailed protocol and give it to them to do' [071, p. 113; p. 3]. Academic scientists also criticised the timing of hub and spoke selection in relation to the release of funds. They felt that funds should have been released prior to hub and spoke selection, which was described as standard academic scientific practice. For example, the same clinical academic involved in UK Biobank described the timing of hub and spoke selection as 'a little bit back to front, it would have been much better to have the grant agreed before things like the home for the hub and the chief executive' [071, p. 113; p. 9].



The funding bodies' decision to involve spokes in protocol development meant that the protocol could not be completed until the hub and spokes were selected. Some representatives of the funding bodies were frustrated regarding the delaying of the funding decision because it delayed hub and spoke selection, which in turn delayed the development of a final protocol. For example a letter from a senior representative of a funding body on 29 November 2000 stated:

[u]nfortunately, until we have a formal decision on funding...we cannot go ahead with identifying either the hub, the chief executive, or the spokes so this will inevitably result in some delay to the implementation of the project...I agree that there would be benefit in identifying the spokes in time to allow them to contribute to the development of the detailed protocol [S600/161 Volume 3; p. 26].

## 4.7 Organisational Changes

**‘More like a sort of standard large research project in that it has a principal investigator’ [E2009, p. 28; p. 1]**

Given the extent of academic scientists’ criticism of the original organisational structure for departing from standard academic scientific practice, it is not surprising that representatives of the funding bodies and UK Biobank Limited justified the organisational changes in August 2005 because they represented standard practice. Academic scientists, particularly spoke members, also acknowledged the nature of the changes as representative of standard academic scientific practice but did not reflect upon their merits. They criticised the process of change as contrary to standard academic scientific practice, arguing that it was not usual for considerable organisational changes to take place following years of effort into implementing an original organisational structure.

### 4.7.1 Organisational changes indicative of standard academic scientific practice

All constituent groups of interviewees described the organisational changes as representing a move back to standard academic scientific practice, which was articulated in terms of control of UK Biobank. The most significant change concerned the role of Rory Collins as the new CEO *and* PI. All constituent groups perceived the development of the PI role as representing standard academic scientific practice in that it facilitated decision making by an individual rather than by groups. For example, a spoke member described how: ‘the Board has gone for a single PI structure, a more conventional structure where the PI has really all the power that he or she needs in order to get things done’ [E2004, p. 14; p. 1]. The term ‘PI’ alone was significant in demonstrating a shift from the business approach to that of the academic scientific approach. Academic scientists used the term, PI, prior to the changes and its official use following the changes was therefore widely accepted by that community as representing standard academic scientific practice (reflected in title quotation in chapter five). For example a spoke member described the changes as making UK Biobank

more like a sort of standard large research project in that it has a principal investigator ...the rest of us are essentially collaborators on the project, I

guess, as opposed to the more sort of quasi-corporate structure that the project had before [E2009, p. 28; p. 1].

Spoke members described this shift from a business approach to an academic scientific approach as one which would benefit UK Biobank. He continued: 'now it does seem to be being organised more as a scientific project and I think that that's probably a better way for it to be organised and as I say hopefully we'll make more progress' [E2009, p. 28; p. 3].

#### 4.7.2 Comparison of the funding bodies' and UK Biobank Limited's perception of the changes with that of spokes

Interviewees' opinions of the changes and the process of change were however polarised. Representatives of the funding bodies and UK Biobank Limited characterised the process of change itself as indicative of standard academic scientific practice and described the development of any scientific resource as subject to change. Despite portraying the process of change as embodying standard academic scientific practice, they tended to minimise its extent. For example, a representative of the funding bodies remarked: 'I think any scientific project evolves as it goes on' [E2008, p. 27; p. 3]. They also took care to underplay any criticism of the previous model, thereby further minimising the extent of change. For example, another representative of the funding bodies stated: 'it's a change of emphasis and it's not really to criticise the way things were done before' [E2003, p. 12; p. 1]. He continued: 'it wasn't revolution, it was evolution' [E2003, p. 12; p. 3]. Representatives of the funding bodies and UK Biobank Limited were positive regarding the process of change and focussed their analysis on their value whilst minimising its extent.

Some spoke members tended to view the organisational changes negatively because of the difficulties caused by the process of change rather than its merits. They criticised the way in which significant changes were made to an organisational structure that academic scientists had invested considerable effort trying to implement, and portrayed this process of change as departing from standard academic scientific practice. Some spoke members avoided consideration of the changes' merits, and portrayed such discussion as irrelevant. Instead their analysis focussed on the difficulties caused by the process of change, which is understandable given the

effect of the changes on their role. Spoke members clearly distinguished the issue of whether or not the changes were valid from the effects of the process of change. For example, a spoke member remarked how there were: ‘lots of reasons to feel miffed irrespective of whether the trial configuration now is appropriate or not’ [E2005, p. 18; p. 1] and said

that may be a legitimate model but it should have been thought of much earlier on and I think, as I said before, that it was very unhelpful to engage us all in this lengthy process only to tell us at the end of it all “well actually we don’t need you” [E2005, p. 18; p. 2].

There was however a deviant case in the sample, which did not follow this pattern. In this case, a spoke member was entirely positive regarding the process of change and discussed the changes' merits. Unlike representatives of the funding bodies and UK Biobank Limited who also analysed the validity of the changes and defended the process of change, this spoke member did not attempt to minimise the changes' extent. For example, he described the process as ‘a bloodless coup’ and the hub and spoke model as ‘that’s a token now, it’s a convenient fiction’ [E2004, p. 14; p. 1]. He portrayed the severity of the changes as a strength and focussed on the positive effect on UK Biobank of an allegedly complete reversal of approach. For example, in describing reaction to the changes he emphasised their extent:

I think everybody was partly stunned and partly relieved...relieved that we knew what the way forward would be and we knew what the lie of the land would be and partly stunned that the change was so complete [E2004, p. 15; p. 4].

Such lack of consistency with the wider sample was evident in the original interview with this interviewee also articulating expectations of spoke membership differently.

## 4.8 Conclusion

Although academic scientists did not explicitly define standard academic scientific practice, a loose model of what it did and did not entail emerged from their criticisms of the establishment of UK Biobank for deviating from it. They presented a standard academic scientific approach to the establishment of UK Biobank as one that would involve the funding decision being based on the production of a finalised protocol rather than on an initial protocol. They argued that academic scientists should have been more involved in initial and ongoing protocol development, as opposed to consultation once key decisions had already been taken. Appointment of a PI, rather than a CEO, was a major part of academic scientists' interpretation of standard academic scientific practice. Their articulation of a standard model also involved a funding figure that included the complete costs for the resource and not just initial set-up costs, and the funding bodies undertaking a secondary role rather than being closely involved in the establishment of UK Biobank. Spoke members in particular cited the establishment of the hub as a company as contrary to standard academic scientific practice. Although spoke members perceived the nature of the organisational changes, particularly the appointment of a PI, as indicative of standard academic scientific practice they argued that the process of such changes was a deviation.

Academic scientists' criticism of the establishment of UK Biobank as departing from standard academic scientific practice is complicated by different understandings of the term. As discussed, they cited a range of models including response-mode funding, a call for proposals and commissioning. There was therefore confusion regarding the nature of standard academic scientific practice, and different academic scientists respectively criticised and praised the same issues for departing and adhering to standard academic scientific practice. Often such different understandings emerged from within the same groups of academic scientists, such as spoke members. For example, some spoke members felt that they were not consulted sufficiently in ongoing protocol development whereas others argued that the protocol should have been finalised prior to their selection; both criticised each position for departing from standard academic scientific practice. Similarly, academic scientists did not define the nature of business practice, with which they associated the appointment of a CEO,

rather than a PI, and establishment of the hub as a company. They associated these aspects with ‘business practice’ and as such stressed their opposition to standard academic scientific practice but did not explain the association. In doing so, academic scientists perceived the establishment of UK Biobank not only as a departure from standard academic scientific practice, but also as a rejection of the academic scientific community in favour of the business community.

Criticism of the establishment of UK Biobank for departing from standard academic scientific practice was a potent feature in academic scientists’ objections to the resource. This criticism encompassed many issues that pervaded the origins and development of UK Biobank, such as consultation, role of the funding bodies, leadership and the organisational structure (particularly the hub and spoke model). These issues recur throughout the remaining findings chapters.

## **Chapter 5**

**‘The local PI’s feel that it is their study and Biobank feel that it is theirs so a tension is still there’ [035; p. 56; p. 8].**

### **Emergent Issues: Control**

#### **5.1 Introduction**

All constituent groups of interviewees, including those involved in each stage of its history, described confusion regarding who was in control of UK Biobank. Given the scale of UK Biobank, all constituent groups stressed the importance of an appropriate level of control over the resource. This chapter will address the explanations of academic scientists, representative of the funding bodies and UK Biobank Limited for the alleged confusion and their opinions of where control lay. It will also explore their perceptions of the type of control most appropriate for UK Biobank. In doing so, it will focus on the following events and issues in a chronological order: protocol development, role of the funding bodies, leadership, organisational structure and organisational changes.

The issue of confusion over control of UK Biobank was responsible for much of the tension between academic scientists and representatives of the funding bodies. Representatives of the funding bodies and academic scientists accused each other of trying to exercise too much control. This chapter will address these accusations and reveal the meanings behind them. All constituent groups articulated the organisational changes as resolving the confusion over control in that they perceived the new CEO *and* PI, Rory Collins, to be the leader of UK Biobank. However, academic scientists and representatives of the funding bodies and UK Biobank Limited interpreted the reasons for the organisational changes differently. I will explore these different explanations for the changes and thereby analyse the issue of control more fully.

## 5.2 Protocol Development

**‘There was a series of key discussion points that we wanted to discuss and basically we were largely prevented from discussing them’ [033; p. 49; p. 7]**

Academic scientists argued that the funding bodies’ role in the protocol development was indicative of their control over it and UK Biobank generally. Members of the PDC criticised the funding bodies for restricting their debate. Some members accused a select group of epidemiologists and representatives of the funding bodies of developing a ‘pre-protocol’ in which key decisions were taken prior to the establishment of the PDC.

### 5.2.1 Criticism of the consultation undertaken with the PDC

PDC members felt constrained by the funding bodies regarding what they could and could not consider. For example a member of the PDC remarked:

There were issues where it was clear that Tom Meade was being driven by George Radda because basically they were very, very cautious, they didn’t want the study to stall because of discussions round and round particular scientific points [033; p. 49; p. 7].

They described being prevented from discussing particular issues such as sample size and age range. For example, the PDC member continued:

There was a series of key discussion points that we wanted to discuss and basically we were largely prevented from discussing them ... one person on the committee was arguing for, well several of us were supporting them including me, that one should be doing an options appraisal ... this was forbidden to be discussed [033; p. 50; p. 8].

Similarly, another member of the PDC discussed the lack of debate on the costs of UK Biobank: ‘there had been explicit non-consideration, I would say, of costing different options for doing the study’ [051; p. 81; p. 9]. They accused the funding bodies of prohibiting their discussions, which reflects criticism of their role in UK Biobank generally. PDC members also cited their experience of the Protocol Development Workshop as evidence of the funding bodies’ control of the consultation process. They felt that discussion was limited by the extent to which key issues had already been decided. For example, the PDC member stated: ‘even at that stage there



was a fair amount of, I use the term ‘didactic’ thinking, about this is the way it’s going to be, there’s going to be a hub and there’s going to be some spokes’ [051; p. 82; p. 5].

Members of the PDC argued that particular issues, such as sample size and age range, were decided prior to their establishment, and thus accused the funding bodies and a select group of epidemiologists of developing a ‘pre-protocol’ prior to their establishment, which limited their deliberations. For example, a member of the PDC described how their discussions were: ‘based upon an outline which had already passed through some form of approval process...what I don’t know is who approved it and on what basis’ [051; p. 81; p. 2]. They felt that the sample size and age range was decided in this ‘pre-protocol’ as 051 continued:

Those who have developed Biobank as a concept were determined that the concept would prevail regardless of scientific input, so the one size fits all, half a million adults, middle-aged throughout the country through primary care [051; p. 81; p. 6].

Some members of the PDC associated the ‘pre-protocol’ with a select group of influential epidemiologists, namely Nick Day, Valerie Beral and Tom Meade. They did not identify the document but given the perception of its authors it is likely they are referring to the Final Report of the EWG. For example, the member of the PDC felt that the ‘pre-protocol’ reflected: ‘a certain amount of opportunism or lobbying or whatever by the three leading epidemiologists’ [051; p. 81; p. 2]. They stressed its influence by referring to the role played by its alleged authors in UK Biobank. For example, the PDC member continued:

It was driven, I am quite sure, from the top through Tom Meade as chairman of the Protocol Development Committee, he was fully compliant with the top-down approach and had a lot of personal investment in seeing the original proposal go forward, I think, because he was part of the team and I suspect he was strongly supported, well I know he was strongly supported by Nick Day because Nick was a member of the Protocol Development Committee and I suspect he was strongly supported by Val Beral when she wasn’t a member but there was this funny arrangement with the secondment of staff...so the original proponents were still really in the driving seat [051; p. 82; p. 9].

He reflected upon the influence of Valerie Beral in terms of the appointment of Emily Banks as protocol writer:

Emily worked for Val Beral in CRUK unit; she was seconded to Tom Meade's unit, to write the protocol...a slightly strange arrangement for someone who's supposed to be an independent person responding to Protocol Committee discussions [051; p. 82; p. 7].

### 5.2.2 Documentary evidence of criticism of the consultation undertaken with the PDC

Documentary evidence of PDC members' criticism of the consultation undertaken with them, specifically that the funding bodies and a select group of epidemiologists decided key aspects of the protocol prior to their establishment, reflects speculation that the funding bodies controlled UK Biobank.

PDC members' accusation that a select group of epidemiologists developed a 'pre-protocol' in which the sample size and age range were decided is reflected in the membership of the 'MRC Post-Genome Challenge Working Group on DNA sample collections and facilities for large-scale genetic typing' (May 29, 1998). This workshop included various influential figures in the origins and development of UK Biobank including George Radda, John Bell and Nick Day [S600/161, Volume 1; p. 2]. Their influence is also reflected in their involvement in the working group. For example, in the second meeting of the group outline proposals were presented by members including Nick Day, John Bell and Valerie Beral. [S600/161, Volume 1; p. 5]. Documentary evidence of PDC members' criticism also includes the minutes of the meetings of the EWG. These minutes demonstrate the extent to which sample size, age range and organisational structure were decided. For example, the notes from the second meeting state how UK Biobank 'should involve several centres around the country (around 5-7) to give efficient coverage of regional variation and to allow inclusion of a wide range of epidemiological expertise' [S600/161, Volume 1; p. 7]. Similarly, in the Final Report of the EWG the proposed age range is very similar to what it became '[t]he cohort for studying diseases of adult life should be aged between about 40 or 45 and 64 years old at recruitment' and the proposed sample size of 500,000 is exactly the same [S600/161 Volume 2; p. 6].

The anonymous comments of twenty-eight reviewers of the EWG Final Report, contained in a document titled ‘Comments received on the Final Report of the Expert Working Group’, also reflect allegations that representatives of the funding bodies and a select group of epidemiologists resolved key aspects regarding the protocol prior to consultation. For example, one reviewer regretted that ‘such an ambitious proposal has been developed to this point without wider consultation with the British epidemiological community, who will be expected to contribute substantially to the establishment of the cohort’ [S600/161 Volume 2; p. 9]. Similarly, the reviewers accused the funding bodies of failing to consider different options regarding the design. For example, one reviewer commented that: ‘[t]he author(s) of the report seem unwilling to discuss other options, save to dismiss them with sweeping generalisations’ [S600/161 Volume 2; p. 9]. Similarly, another remarked: ‘I would have preferred a wider discussion of the strategic scientific issues BEFORE committing such a huge effort in one particular direction’ [S600/161 Volume 2; p. 10].

Consideration of the IPC was a particularly controversial episode in the PDC, which reflected criticism of the control exercised by the funding bodies over the Committee. For example, the minutes of the fourth meeting of the committee in October 2001 refer to the role of the funding bodies in the decision that the IPC would be considered separately from the main protocol stated:

Sir George had strongly recommended that the committee focus primarily on producing a protocol and a sound, well-argued case for the core data collection on the whole large cohort. The Committee could recommend the inclusion of an IPC but the proposal should be clearly separate ... Dr Doyle reported that Dr Dexter was of the same view: any proposal for an IPC should be separate from the proposal for the large cohort [D550/33 Volume 2; p. 17].

PDC members’ reaction to the decision reveals the tension in the Committee regarding control. For example, in response to the circulation of the decision to consider the protocols separately prior to the Committee’s next meeting, a member of the IPC sub-group wrote in an email to the chair of the Committee:

I think this demonstrates your commitment to ensuring that the Protocol Development Committee is actually a meaningful body with a real purpose

rather than just a rubber stamping mechanism for decisions that are really being taken elsewhere [S600/174 Volume 2; p. 17].

He continued by asserting his belief that the IPC should be presented to reviewers 'as one potential component WHICH IS ON AN EQUAL POTENTIAL FUNDING FOOTING to any other potential component of the study [his emphasis]' [S600/174 Volume 2; p. 17]. The funding bodies' decision not to send the IPC protocol to peer reviewers in the form prepared by the IPC sub-group, but to have it re-written and shortened by Emily Banks, Frances Rawle and other funding body representatives and sent with a letter of recommendation also reflected the funding bodies control. PDC members expressed support for the decision itself. For example a member stated: 'I am prepared to accept that this decision may be defended in terms of overall strategy'. However they were offended by the implication that they prepared the IPC protocol as a threat to the main protocol. For example, a member commented: 'I am personally saddened by the implication that our protocol was in any sense written in a manner that deliberately undermined the main protocol' [S600/174 Volume 2; p. 18].

### 5.3 Funding bodies

**‘Very broadly you do better if you actually give support to good and entrepreneurial and creative scientists than if you say ‘I’ve hired these good, creative, entrepreneurial scientists-will you please now do this, this and this?’ [071; p. 116; p. 6].**

Academic scientists attributed the alleged confusion over control of UK Biobank to the role undertaken by the funding bodies, which they criticised as controlling. They differentiated between the relative influences of the two main funding bodies. Some felt that the Wellcome Trust was in control whereas other argued that the MRC held the dominant position. Representatives of the funding bodies denied exerting such control.

#### 5.3.1 Criticism of the funding bodies’ role

Academic scientists criticised the funding bodies for being too much in control of UK Biobank and argued that funders were too involved in its origins and development. They felt the inspiration for the resource lay with the funding bodies rather than academic scientists. For example, a spoke member remarked: ‘There is a risk in running a study that is not hypothesis driven or not coming from the ranks of scientists but is driven from the top’ [024; p. 32; p. 3]. Academic scientists attributed the tension between representatives of the funding bodies and academic scientists to the degree of control exerted by the former in the origins of the idea. For example, a member of the EWG commented:

It’s [science] driven by passion and ideas and there’s clearly a great idea, UK Biobank is in principle a great idea but it needs to be driven by scientific passion and curiosity. You haven’t had a sense of ownership and how you achieve that is not trivial...so I think that it’s not surprising that there has been a considerable amount of tension generated by the responsibility of the funders on the one hand to set something up in a very transparent, a financially transparent, mechanistically transparent way and yet find a way in which the scientists can be engaged with that [062; p. 102; p. 7].

They argued that the funding bodies, rather than the hub, were really in control of UK Biobank. For example, a spoke member reflected:

Whenever we've raised something that we think should be questioned and we are given back the message the funders won't countenance it, it gives us the impression that the funders are keeping a very tight rein on the project [0102; p. 134; p. 6].

Similarly, another spoke member remarked: 'they've been far too intrusive and I think the degree of control has been frankly lamentable. It's very counter productive' [0800; p. 194; p. 4]. Academic scientists criticised the funding bodies' influence over the hub and specifically over the former CEO, John Newton. For example, a member of the PDC commented:

The CEO was constantly being put under pressure to make sure that particular deadlines, timelines were being met that scientifically were clearly not sensible, and basically if the funders had just stood back and said "alright, we accept the advice from the scientists that these are unreasonable we're therefore not going to put pressure on the CEO to make sure that they meet them" that would have made things go a lot easier [033; p. 52; p. 6].

Spoke members suggested the optimal role of funding bodies to be one that did not interfere with the scientists' role. For example, one spoke member stated that the funding bodies 'should stand back and let the scientists get on with it' [0800; p. 194; p. 3]. Similarly, a clinical academic involved in UK Biobank reflected:

Funding agencies do their best work when they have good, novel, original ideas of things that might be worth supporting but then once they've decided to do it, they've decided to do this piece of work or pieces of work, whichever pieces they're going to support, adopt a very hands-off approach because research does not do well with a heavy hands-on approach [071; p. 115; p. 6].

Academic scientists emphasised the preferred role of support, as opposed to control, by funders of academic scientists. For example, 071 continued:

Very broadly you do better if you actually give support to good and entrepreneurial and creative scientists than if you say "I've hired these good, creative, entrepreneurial scientists-will you please now do this, this and this?" [071; p. 116; p. 6].

Academic scientists accused the funding bodies of taking key decisions regarding the scientific design of UK Biobank, such as the sample size. For example, a spoke member commented:

The funders are particularly concerned with scale and in discussions of having fewer participants and more detailed information the funders have always stuck to the scale of the project...the project is not scientifically driven, it is driven from a marketing point of view, political with a small p. They do not want a better study with smaller numbers, they want to be the 'largest', they are just not interested in anything smaller [030; p. 42; p. 2].

He went on to stress the power of the funding bodies to set the agenda regarding discussions of the design:

The funders always made it clear that the scale of the study would not change...large numbers offset poor quality in studies, you can get away with more if there are larger numbers...it ruins the quality but does not stop you publishing [030; p. 43; p. 2].

Similarly, a member of the scientific community outwith UK Biobank commented:

My understanding is that this is off-limits, half a million was decided in the original work on purely political grounds, so now the people who are trying to get together the protocol...they have their hands tied by history because there's been press releases, because we've had George Radda on the radio saying it's going to be half a million people...that is set in stone, nobody can change it and that's a pity because there are good scientists out there who might have come up with a better solution [0900; p. 198; p. 14].

As discussed in the previous section, PDC members accused the funding bodies of exerting control over their deliberations. For example, a member of the PDC remarked:

Several times it emerged in discussions that he [Tom Meade] has received this message very firmly on high...the implication is that there was still very firm direction centrally from George Radda, Mike Dexter and possibly others who'd been involved with the original proposal [051; p. 83; p. 6].

Academic scientists also accused the funding bodies of taking organisational decisions, such as those regarding the hub and spoke model and the BoD. They argued that the funding bodies, rather than the scientists, were responsible for the hub and spoke model. For example, a member of the EWG remarked:

In terms of the way the project was set up, I can't really comment except that it went into the offices of the Wellcome Trust and the MRC and to my

knowledge, the model for how it was to be set-up did not arrive out of a consensus view offered by the study proponents but by the organisers and the funders, so it was driven by the funders, not by the scientists [062; p. 102; p. 6].

Academic scientists argued that the funding bodies controlled the appointment of committees within the organisational structure. For example, a spoke member accused the funding bodies of refusing to allow an Implementation Group composed of the spoke leads to form:

The RCC leads are not actually funded and not given the remit, not given permission to do it. They volunteered their time to have more meetings but the funders did not want them to do that and wanted one of their own, which was fine but it took ages [030; p. 44; p. 4].

They also criticised the role of the funding bodies within the organisational structure, specifically in the BoD. Given the involvement of representatives of the funding bodies, academic scientists questioned the independence of the Board. For example, a clinical academic involved in UK Biobank commented:

It's not a truly independent company because there are three directors who come from the funding agencies, of course, very properly, their interest in coming from the funding agencies is declared but it means that the Board is looking over its shoulder all the time, what the funding agencies would want [071; p. 116; p. 8].

Similarly, a spoke member remarked: 'the Board is largely, not necessarily governed, but largely influenced by the views of the funders' [0102; p. 134; p. 6]. Members of the BoD, whilst acknowledging the role of the funding bodies on the Board, explained how it diminished as the Board developed. For example, a member of the BoD commented:

The Board has to be aware of the need to meet the requirements of the funders at all times. However the funders are beginning to have more trust...I think the funders are beginning to focus elsewhere and leave Biobank to get on with business [070; p. 108; p. 8].

Some academic scientists justified the alleged control exerted by the funding bodies over UK Biobank because of their financial obligations and their importance in getting the idea up and running. They referred to the large sums of money involved in



UK Biobank as an explanation for such an active role. For example, a member of the EWG commented: ‘If you take a single investment the risk of failure is too high to have it anything other than under close management scrutiny’ [062; p. 102; p. 9]. Academic scientists also referred to the funding bodies’ requirement to justify the investment to their senior groups. For example, a clinical academic involved in UK Biobank stated:

It’s an awful lot of money and it is their money, they’re responsible publicly for it...they’ve got to retain a delicate, light touch but very clear understanding of what’s going on so that they’re guarding their money but not slowing things down [071; p. 116; p. 6].

They acknowledged the importance of the funding bodies’ involvement in allowing UK Biobank to happen. For example, a member of the PDC remarked: ‘from George Radda’s point of view first of all he was correct to be concerned that if he hadn’t had a strong drive from the top it might have got nowhere’ [033; p. 52; p. 6]. Academic scientists acknowledged the importance of support for the idea from the scientific community but stressed the significance of the role undertaken by the funding bodies in making UK Biobank happen. For example, the clinical academic quoted above continued:

The funders wanted it done and there were a number of people in the scientific community who also felt, yes, it was worth doing, the scientific community might have thought it would be a good idea but if the Wellcome or the MRC hadn’t said “we’re starting to think this might be a good idea” they’d have thought they would have missed their chance for funding [071; p. 115; p. 4].

### 5.3.2 Relative influence of the two main funding bodies

Academic scientists speculated as to the relative influence of the two main funding bodies, the MRC and the Wellcome Trust, on UK Biobank. Some felt that the MRC was the most influential funding body whilst others argued that the Wellcome Trust exercised greater control.

Those who identified the Wellcome Trust as the dominant funding body referred to its role in the development of the resource. For example, a member of the BoD commented: ‘my understanding is and was that it was very much driven by Wellcome

and it is still the main kind of driving force behind it' [070; p. 107; p. 1]. He felt that the Wellcome Trust was responsible for major decisions surrounding UK Biobank:

The joint funding agreement between the Board and the funders was drawn up by the lawyers in the Wellcome Trust...I would imagine the final decision on the name is taken by the Wellcome Trust, the final policy on the structures for instance, the letters inviting me to be on the main Board came from the Wellcome...if you wanted to know where the key decisions were made I'd go to the top of the Wellcome [070; p. 107; p. 14].

In describing the greater influence of one funding body over the other, some academic scientists criticised the more influential body. For example, a clinical academic involved in UK Biobank remarked:

If there's any one reason why it was set up that way it's because, my perception is that the dominant voice in deciding the structure and how it was done was the Wellcome rather than the MRC and the Wellcome Trust sadly is characterised by having quite a lot of staff who've never run anything large scale [071; p. 114; p. 4].

Others argued that the MRC were more influential on account of their involvement in the origins of the idea. For example, a member of the scientific community outwith UK Biobank remarked how

one got the feeling with the MRC that it wasn't a question of they were wanting to find out whether this should be done or not, they had decided this was going to be done, as I say they'd released press releases, they'd decided this was going to be done [0900; p. 195; p. 2].

He contrasted the influence of the MRC with that of the Wellcome Trust whom he felt were 'sort of backed into a corner by then because, you know, they'd agreed the funding in principle without their normal process of peer review' [0900; p. 195; p. 2].

### 5.3.3 Funding bodies' perceptions of their role

Representatives of the funding bodies downplayed the significance of their role in the origins and development of UK Biobank. They argued that following the establishment of UK Biobank Limited their role was minimal, and reflected upon the problems of being too involved. For example, a representative of the funding bodies remarked: 'The staff of the funders can take it only so far but eventually you've got to

pass it onto people who are going to take the project forward' [040; p. 59; p. 15]. Similarly, another representative of the funding bodies commented: 'having handed over independence, having got a governance board with very competent and powerful people on it I think most of us have wanted to take a relatively back seat' [E2011; p. 33; p. 3]. He continued by stressing the dangers of the funding bodies taking an active role:

It would be double jeopardy in the management structure, I mean you can't expect people to take on jobs that normally assign to them governance and managing responsibilities only to have other organisations and other people, particularly people with the purse strings coming in and meddling when they want to [E2011; p. 33; p. 4].

They did however acknowledge the necessity of some level of involvement whilst not exerting too much influence. Representatives of the funding bodies referred to the difficulty of adapting their role to the changing requirements of the resource and argued that prior to the establishment of the hub they needed to be significantly involved. For example, a representative of the funding bodies remarked:

Our role leading up to the establishment of the company and all that was a much more hands-on, much more directive role. I think if you are going to set up a company to do it and ensure it's got the right governance structures then you don't sit on its neck all the time. I feel that we have to learn on both sides how quite to deal with it at arm's length and that's been a learning curve for all of us [043; p. 71; p. 12].

They also defended their involvement following the set up of UK Biobank Limited and argued that they were still required. For example, the representative of the funding bodies continued:

There is still some need I think for us to be involved in stakeholder engagement, ensuring that we are getting the best value for money from Biobank and that Biobank's providing what the scientific community wants and that can't be solely down to Biobank and its objectives [043; p. 71; p. 12].

In defending their involvement, representatives of the funding bodies discussed how academic scientists, as opposed to themselves, drove the idea for the resource. For example, a representative of the funding bodies remarked:

Although this required a lot of work from the top actually this was what the scientific community wanted...this project, by people who didn't understand it, was seen as, if you like, a project driven by the two organisations as opposed to by the scientific community. We responded to the scientific community wishing to do something like this and was very clear early on that's where the motivation came from [044; p. 75; p. 8].

He continued: 'Yeah we had to implement it but the motivations came from the scientists' [044; p. 75; p. 9]. They also stressed their importance in channelling the activities of the academic scientific community and making UK Biobank happen. For example, the representative of the funding bodies commented:

It's not been plain sailing all along but I think it tells us that one can do this kind of science given the will and you do need people who are going to drive it and usually I think it has to be driven by the scientists themselves wanting to, the scientific community is not well organised so that the funders can organise them or have to organise them and unless there is a real driving force within the funding organisations these things won't happen [044; p. 76; p. 11].

Representatives of the funding bodies further justified their role on account of their obligations to their organisations to ensure the security of the financial investment. For example, a representative of the funding bodies commented:

It's not something that the Medical Research Council or even the Wellcome would probably feel comfortable simply delegating to a group of scientific champions... in the after analysis the Wellcome has its trustees, the MRC has its council and government to whom they are accountable [041; p. 61; p. 6].

They also referred to their legal obligations as members of the company itself, UK Biobank Limited, in maintaining a role in UK Biobank. For example, a representative of the funding bodies remarked:

Biobank is not a body that's completely at arm's length, legally it's a company limited by guarantee with members and the members are the Wellcome Trust and the MRC and the structure of it, the corporate structure of it means that they are required to agree to all sorts of major decisions [072; p. 118; p. 4].

It could be argued however that these arguments contrast with their presentations of the company, UK Biobank Limited, as a separate entity, independent of the funding bodies. For example, representatives of the funding bodies referred to the importance

of creating an entity not under the control of any particular individual or group (including the funding bodies) in justifying their decision to establish the hub as a charitable company, UK Biobank Limited.

## 5.4 Leadership

**‘I can’t take the decision, somebody at Biobank or on one of the committees and I’m not quite sure who the hell it is, would *take* that decision, so it’s a power thing really, I’m powered to *make* decisions but not to *take* decisions [his emphasis]’ [0202; p. 150; p. 7].**

All constituent groups of interviewees attributed the alleged confusion over control of UK Biobank to a lack of leadership but they articulated it differently. Academic scientists articulated the lack of leadership as a lack of an individual (as opposed to committee) and academic scientific leadership, whereas representatives of the funding bodies and UK Biobank Limited articulated it as a lack of managerial leadership.

### 5.4.1 Lack of a leader

Academic scientists struggled to identify a leader of UK Biobank and attributed the confusion over control to this difficulty. For example, a spoke member commented: ‘I’m not sure it has got a clear driver... I’m not clear who is the leader on it’ [023; p. 29; p. 3] and another spoke member remarked that ‘it’s difficult to know exactly who is behind certain things that happen within UK Biobank’ [0105; p. 141; p. 5]. Some academic scientists acknowledged leadership positions, such as the CEO or Chair of the Science Committee, but did not identify them as leaders. For example, a spoke member stated: ‘I know John Newton was the CEO but we didn’t have a sort of complete, I think feeling that there was someone at the helm’ [0203; p. 153; p. 5]. Academic scientists were surprised that an endeavour of the scale of UK Biobank not only lacked a leader wholly responsible for delivering the resource but also lacked a product champion. For example, a member of the EWG remarked: ‘what this has not had is a very vocal, charismatic, single product champion who can get, you know, universal respect’ [061; p. 96; p. 7] and a spoke member stated: ‘it’s the kind of project that you think might well have a name behind it, someone who you could say this person is really the figurehead of this’ [0103; p. 136; p. 5]. Some academic scientists strongly connected the position of leader responsible for delivering the resource with that of scientific champion acting as the public face. For example, a member of the EWG commented:

I think also probably what was difficult for the project was that when it was formalised there was actually no real leader...John Newton had no history of

attachment to the project. He was never a champion. John Bell was never going to champion it because it was always something that he felt strongly about but it was secondary to his role as Regius Professor of Medicine. No other person was so clearly the outstanding leader of the project that they could justifiably stand up and say “This is what we’re going to do, and this is my team of people that will do it with me” [062; p. 101; p. 17].

Academic scientists criticised the lack of a leader as it complicated decision making, and thereby contributed toward the confusion over control. They were frustrated over the anonymity of decision takers and felt powerless as a result. For example, a spoke member remarked:

There is no clear process if something is felt to be not up to scratch. It is not clear who to go to or who is making the final decision...you find yourself in a difficult position as you have no control and everything has to be agreed so you can only strongly recommend something and you can’t make the final decision [035; p. 56; p. 8].

Spoke members in particular were frustrated that they were involved in evaluating decisions but were not given the authority to take decisions, exacerbated by not knowing who was taking these decisions. For example, a spoke member distinguished between decision making that involved spoke members and decision taking that did not involve spoke members: ‘I wonder, not sometimes wonder, constantly wonder, who are, we know who the decision makers are in this organisation but who are the decision takers?’ [0202; p. 150; p. 6]. He continued

I can’t take the decision, somebody at Biobank or on one of the committees and I’m not quite sure who the hell it is, would *take* that decision, so it’s a power thing really, I’m powered to make decisions but not to take decisions [0202; p. 150; p. 7].

They did not know who was in control of UK Biobank because they did not know who was responsible for decision making.

#### 5.4.2 Leadership by committee rather than by an individual

All constituent groups of interviewees differentiated between leadership by committee and leadership by an individual, and associated UK Biobank with the former on account of the consultation involved in its origins and development.

Academic scientists criticised leadership by committee and held it responsible for the confusion over control of UK Biobank. They associated it with the difficulty of decision making and the consequent delay in implementing the resource. For example, a spoke member commented:

Whilst there needs to be a lot of consultation, there still needs to be a very small body or maybe an individual at the end who makes the sort of final decision about what direction the project's heading in, otherwise it tends to go backwards and forwards [E2000; p. 1; p. 1].

Similarly, another spoke member stated:

The development of a research proposal needs an element of leadership by definition and I think it's very, very difficult for what Biobank is trying to do at the moment and that goes at every single level, really. I know that there have been very robust methodological debates around what kind of approach should be taken, and there is a lot of discussion around what measures should be included in the questionnaire and it's difficult to resolve those sorts of arguments by committee [0201; p. 146; p. 4].

Even those spoke members who supported the leadership by committee approach in theory were sceptical. For example, a spoke member stated:

It lets all the scientists have a say and it would not work if it was just one scientist at the top dictating but there is a danger of it being too democratic, with the revisiting of decisions there is a danger of just going round and round [027; p. 40; p. 3].

Academic scientists pointed to the difficulty of managing multiple and vested interests in the leadership by committee approach. They associated this difficulty with the confusion over control of UK Biobank, arguing that leadership by committee allowed different groups to exert undue influence. For example, a spoke member commented:

In one sense the Executive Officers are driving it and in another sense the Board regard themselves as the drivers, so there are multiple major



stakeholder groups both within Biobank and I think outside, I think the MRC and Wellcome would say they're driving it and the Department of Health ... they're doing it at different levels rather than there's one person or one group of people who does it at all levels [0102; p. 133; p. 5].

He continued reflecting upon the need for such a person:

If that person had the weight and the trust of the various major groupings that I described then inevitably that person could then make what would be seen to be appropriate decisions and respectable decisions to the various groups [0102; p. 133; p. 5].

Representatives of the funding bodies largely supported the leadership by committee approach and stressed the importance of the collaboration it fostered. For example, a representative of the funding bodies remarked:

The ethos at the time and I don't think we've moved away from this is to achieve an integration of Biobank across all of the relevant interests in UK academia and to get the best UK departments and the most appropriate involved with Biobank [043; p. 69; p. 10].

They feared that leadership by an individual would result in one person wielding too much control over UK Biobank. Although representatives of the funding bodies acknowledged the difficulties involved in not having an identifiable leader they remained cautious of such a figure. For example, a representative of the funding bodies commented: 'it's suffered through lack of scientific champions along the way or really people identifiable as scientific champions' [043; p. 70; p. 17]. Yet he warned of the dangers of leadership by an individual:

I'm not quite sure mechanistically how you would try in that kind of context to achieve scientific champions because with scientific champions comes vested interest, with scientific champions comes a lot of other baggage with regard to "I will design it this way and I'll do it my way" rather than trying to create a resource that has an impact and relevance right across a bigger sphere of people [043; p. 70; p. 17].

The funding bodies' caution reflects academic scientists' criticism of their role in UK Biobank. Academic scientists felt that the funding bodies exerted too much influence over the resource to prevent an individual or another single group taking control.

Representatives of UK Biobank Limited associated leadership by committee with the academic scientific community and leadership by an individual as representing business practice. They therefore attributed the confusion over control of UK Biobank to the adoption of academic scientific practice in the form of leadership by committee. For example, a representative of UK Biobank Limited commented: ‘I have had a lot to learn about the academic environment and the way in which things are done, which is very different to the places that I’ve come from’ [0600; p. 180; p. 1]. He explained how he came from ‘a background of strong project management that is not an approach that academics and scientists necessarily take’ and how

the environment that we’ve worked in is fundamentally based on things like contracts and out-sourcing arrangements whereas this environment is much more about collaborative working, which is less easy to express within the sort of contracts and planning arrangements that we’ve been used to working in [0600; p. 180; p. 2].

#### 5.4.3 Academic scientific and managerial leadership

Academic scientists criticised UK Biobank for representing managerial leadership and associated this with the confusion regarding control of the resource, whereas representatives of the funding bodies and UK Biobank Limited criticised UK Biobank for representing scientific leadership and as such contributing to the confusion over control. These different articulations of the type of leadership involved in UK Biobank reflect the confusion over understandings of standard academic scientific practice and business practice explored in chapter four.

Academic scientists identified the leadership involved in UK Biobank as managerial on account of the professional background of those employed at the hub in that they were not academic scientists. They argued that managerial leadership was inappropriate for a scientific endeavour and responsible for some of the difficulties involved in decision making. For example, a spoke member remarked: ‘[a representative of UK Biobank Limited] background is not sort of scientific epidemiological background so it was more leadership from the point of view I think of management’ [E2000; p. 1; p. 1]. He continued by asserting the importance of scientific rather than managerial leadership:

It's very difficult for someone who doesn't have a scientific or an epidemiological background to lead the project because decisions need to be made on some scientific issues as well that have a very large impact on the overall management, the viability of the project from a financial point of view as well and obviously the feasibility of this study ... it wasn't the sort of leadership that I think it needed [E2000; p. 2; p. 2].

Representatives of the funding bodies and UK Biobank Limited criticised the leadership involved in UK Biobank as scientific rather than managerial. They identified scientific leadership with extensive consultation and the existence of multiple, vested interests. For example, a representative of the funding bodies commented: 'there was a corporate spirit that was missing, the idea of collecting this data for the common good slowly disappeared and so you've got people's vested interests coming along' [042; p. 67; p. 16]. They identified managerial leadership as leadership by an individual and associated it with strong organisational skills. The representative of the funding bodies continued:

We needed someone with a good organisational background who was able to adopt a can-do mentality that was able to organise people, able to actually put people in place to go out, do recruitment to answer questions, just kind of, not agonise on 'am I collecting the right data or something?' ... The key thing that was missing right from the word go was a strong manager, right from the word go, and a manager that had respect from the academic community, from the funders, a manager that was able to make executive decisions from the word go and that didn't happen. It was all this horrible management by committee, never works [042; p. 67; p. 17].

Interestingly, this interviewee's criticism of scientific leadership interpreted as consultative contradicts representatives of the funding bodies' support for leadership by committee and wariness of individual leadership.

## 5.5 Organisational Structure

**‘They choose it [the establishment of a hub as a charitable company] to sort of remove from them [the funding bodies] the power of control of it [UK Biobank], so it’s separate, it’s not the MRC’s project, it’s not Wellcome’s project, it’s not the Department of Health’s—it’s Biobank’s project’ [0503; p. 178; p. 9]**

Academic scientists attributed the alleged confusion over control of UK Biobank to the organisational structure, particularly the hub and spoke model. They argued that the role and responsibilities of the hub and spokes were not clear. Representatives of the funding bodies established the hub as a company to ensure that it was free from any particular individual or group’s control.

### 5.5.1 Establishment of the hub as a company

Representatives of the funding bodies argued that the hub should be established as an entity separate from the funding bodies, the Government and any single organisation (such as a university) to ensure its independence. They felt that establishing the hub as a charitable company would ensure such independence, prevent any university or existing organisation exerting undue influence, and grant it a strong separate identity. For example, a representative of funding bodies commented:

we believe it [establishment of the hub as a company] gives, especially with this type of database, patients who consent to be part of the study reassurance that this is not a company that’s going to make profit out of it, it’s not a Government, a solely Government sponsored organisation that they might begin to feel a little bit, in the future anyway, not happy with, some kind of Government sponsored thing for patients is a fear that they are not giving it to a truly independent body and use it in the best interests, not simply to them but of the other people in the UK [040; p. 60; p. 11].

Similarly, another representative of the funding bodies remarked:

It wasn’t easy to see how you could create the kind of resource that you wanted while simply giving a grant to one of the organisations in the field. You’d have ended up with something that belonged more to a university than it did to the national research enterprise but then also we needed a model

through which a set of funders could operate and feel comfortable with [072; p. 119; p. 6].

A further representative of the funding bodies stated that ‘it was important ... to have an independent organisation that would gain a life of its own’ [043; p. 69; p. 9].

The funding bodies’ arguments were evident in the documents relating to Site Visit Reports for the hub bidding process. For example, bids were criticised for not appreciating the proposed independence of the hub and praised for acknowledging such independence: ‘there was an impression that overwhelming academic influence could easily overpower the Hub’s autonomy’ and ‘no clear idea of Hub-Spoke separation’ [D550/12 Volume 1; p. 35]. On the other hand, bids were praised for ‘clear vision of the Hub-Spoke separation’ and ‘clear vision of Hub independence/autonomy’ [D550/12 Volume 1; p. 35].

Spoke members acknowledged the funding bodies’ wish to establish the hub as an independent entity to prevent another group controlling UK Biobank. For example, a spoke member commented: ‘they choose it to sort of remove from them the power of control of it, so it’s separate, it’s not the MRC’s project, it’s not Wellcome’s project, it’s not the Department of Health’s – it’s Biobank’s project’ [0503; p. 178; p. 9].

### 5.5.2 The ‘hub’ and ‘spoke’ model

Academic scientists and some representatives of UK Biobank Limited criticised the hub and spoke model for creating confusion over control of UK Biobank. They argued that the number and size of the spokes meant that too many people were involved in the resource and attributed difficulties faced in decision making to such involvement. For example, a representative of UK Biobank Limited commented:

We’ve got too many people...it should have been given to a small group of scientists...we’ve got 23 universities involved, how many professors do you need to change a light bulb? The answer is one person does it well, 23 people discuss how to do it and never do it...you have a large number of people not properly involved in the project, chipping in bits and pieces from time to time and it’s desperately inefficient and very unsatisfying [010; p. 4; p. 6].

Similarly, a clinical academic involved in UK Biobank remarked:

You've now got this big structure, a spider's web of hub and spokes with a lot of people involved ...it's much more difficult if you've got a very large group coming up with their idea. This is the kind of research that is perhaps better done by very small groups [071; p. 115; p. 5].

Given the involvement of numerous and large groups, academic scientists described the difficulty of appeasing multiple and vested interests in making decisions. For example, a spoke member commented: 'It's a bureaucrat's nightmare this study, decision making is very diffused, it's not clear...the same material was being examined repeatedly and usually always leading to the same conclusion' [025; p. 36; p. 4].

Academic scientists argued that the committees were too large and described the difficulty of reaching consensus amongst the Science Committee and BoD particularly. For example, 025 continued: 'it's too bureaucratic, you have funders, you have Biobank Board of Directors, then you have the Science Committee, then you have an Implementation Committee and you have numerous sub-committees' [025; p. 36; p. 4]. Similarly, another spoke member commented 'The delays were also because of the science committee being too big and unwieldy' [030; p. 43; p. 4]. Academic scientists also cited the difficulty of appeasing multiple and vested interests on account of the involvement of numerous and large committees. For example, a member of the BoD remarked:

The science committee is still and will always be I think a group of people who have a large interest in making the project work but also their own personal hobby-horses to ride and their reputations to protect [070; p. 111; p. 13].

Unlike other academic scientists, he argued that the BoD did not suffer the problems of multiple and vested interests associated with the Science Committee in particular as it adopted a 'corporate approach'. His comments thereby resonate with the funding bodies' arguments that managerial leadership was more appropriate than scientific leadership. For example, he praised the BoD for adopting a corporate approach and criticised the Science Committee for not adopting that approach:

there are still people there [in the Science Committee] who will be very corporate at times and very un-corporate at other times when their particular interests come to the surface ... it [the BoD] was corporate right from the start

because people weren't appointed because they had hobby-horses but they were appointed because they had to do business [070; p. 111; p. 13].

Academic scientists, in particular spoke members, referred to the pressure placed on the former CEO, John Newton, in handling the multiple and vested interests of the committees and funding bodies: 'I know John Newton is chief exec but I'm not sure I think he's being pulled in lots of different directions. There are lots of people with their own agendas here' [023; p. 29; p. 3]. Given the organisational structure, he spoke of the difficulties faced by John Newton in asserting his authority:

John I think has had an incredibly difficult time just establishing his offices, his infrastructure etc...I'm not sure that John either feels able to or it's his remit to actually say "this is what we're going to do". So it's I think it is struggling a bit because of that [023; p. 29; p. 4].

Academic scientists identified the funding bodies as a further group asserting a vested interest in UK Biobank. For example, a spoke member implicated them in the pressures placed on John Newton:

I felt John Newton, I thought, did a very good job. My impression was that as Chief Executive he was likely to be being pulled in all sorts of directions and didn't have the freedom possibly to make the decisions, there were other, you know, powerful figures within Biobank who were perhaps controlling the purse strings and perhaps he didn't have the authority or the freedom to make the decisions that needed to be made for Biobank [0104; p. 139; p. 3].

They argued that the alleged confusion over control allowed these multiple and vested interests to exert their control over UK Biobank.

Academic scientists implicated the hub and spoke model itself in the tensions between the hub and the spokes. Given the extent to which spokes were involved in protocol development and the importance of their function in delivery of the resource, academic scientists argued that regulating their role was problematic. For example, a clinical academic involved in UK Biobank commented:

If you define something as a spoke, you know, an essential part of the overall structure then it becomes very difficult to use a spoke just as a sample and patient subject collection entity, it becomes a body that really wants to get involved as part of the research [071; p. 115; p. 7].

Some academic scientists argued that the hub encountered difficulties in asserting its control over the resource on account of the funding bodies involvement, which contributed to the tension in the model. For example, 071 continued:

You create a structure whereby the chief executive and the company have to go back and get approval from the funders for any number of relatively small amounts of decisions...you've created an entity which should be able to move fast and be responsive and independent and then you slow it down by making it financially utterly dependent [071; p. 114; p. 3].

### 5.5.3 Role of the hub and spokes

All constituent groups of interviewees associated the ambiguity over control of UK Biobank with the confusion regarding the role of the hub and spokes. They articulated this confusion largely in terms of the authority that the hub held over the spokes and the resource generally. This perceived authority accounted for much of the tension between the hub and spokes. Academic scientists contested the hub's authority over the spokes whereas representatives of the funding bodies and UK Biobank Limited argued that the hub should have had more authority over them. Academic scientists were however divided on this occasion as members of the BoD felt that the hub should have held a dominant position over the spokes whereas spoke members criticised such a role.

Representatives of the funding bodies, UK Biobank Limited and the BoD argued that the hub experienced difficulties in asserting its control over UK Biobank because of the allegedly controlling role undertaken by spokes, which they criticised. For example, a representative of the funding bodies claimed that the academic scientific community

didn't like the idea of the central unit collecting all the data and coordinating its collection and just these units out in the periphery ... so you begin to subvert this purist hub and spoke model into sorts of centres that were located around the regions that were actually heavily involved in the utilisation of the data and doing their own little research projects [042; p. 66; p. 11].

Similarly, a member of the BoD remarked:



The academic community are only one of the stakeholders and in some ways I suspect they've been given too much of a stake and that's one of the errors around the RCC concept. It put too much concentrated depth of influence in the hands of the RCCs [070; p. 111; p. 12].

Representatives of the funding bodies, UK Biobank Limited and the BoD praised the development of the hub and spoke relationship as the hub increased its control over UK Biobank whilst the spokes' influence diminished. For example, the member of the BoD continued:

Originally there was going to be a lot of regional flavour ...gradually it's coming up that everybody will follow the same protocol and do a very similar thing...there will be some flexibility but it's going to be based not on the whim of the people locally but on what is actually going to work to get the people in [070; p. 110; p. 6].

They interpreted this development as representing the adoption of a centralised model, which they defended. For example, another member of the BoD remarked:

There is a bit of a power struggle there and I think that one of the things that has changed in my mind is that it has to be quite strongly managed and we have to have a centralised approach to things, now that's against my normal way of thinking but I think in this case to ensure authenticity and to achieve the economies of scale [013; p. 17; p. 5].

Representatives of funding bodies, UK Biobank Limited and members of the BoD also associated the difficulties of asserting the hub's control with the way in which it was established. They cited the practical difficulties of establishing the hub and the problematic sequence of events by which it was set up. For example, a representative of UK Biobank Limited commented: 'we had no infrastructure at all, absolutely no infrastructure, nothing, not even a secretary or an email account' [010; p. 6; p. 7]. They felt that the hub should have been established and developed prior to the appointment of the CEO and spokes. For example, a clinical academic involved in UK Biobank remarked:

You've appointed the person to run it before he knows exactly what he's going to run and it has the fault that you've appointed both the hub and spokes who are told that they've got to work together but it's not clear who is responsible for what and it doesn't give an exclusive centre for the person or

the group who will actually make the final decision for what the scientific protocol is going to be and the nuts and bolts of ethics and so on [071; p. 113; p. 3].

They also associated the appointment of the BoD, the main authoritative body, following the establishment of the other committees and spokes with the difficulty of asserting the hub's control. For example, 071 continued: 'you've got a company which is parachuted in somewhere around the end of the process, without them as a board having been involved in developing it to this stage' [071; p. 113; p. 3].

Spoke members criticised the control exercised by the hub over the spokes, and the resource generally, as inappropriate. They stressed the power of the hub over the spokes and conceived of the model very much as centralised; for example, a spoke member remarked:

They are being very strongly dictated to by the centre and really not being allowed to contribute in a meaningful way to the science and that means the whole thing becomes untenable for university organisations [0800; p. 194; p. 5].

Another spoke member commented: 'we're not being allowed, the spokes, to really drive the agenda, the agenda is coming from the centre and it seems to be getting increasingly centralised, which is a little bit worrying' [023; p. 30; p. 3]. They described feeling disenfranchised through a lack of genuine consultation in decision making. For example, a spoke member commented:

The decisions around how it is done and the strategy and the protocol they took it to be the Executive Officer's domain and not to do with the RCCs, so they would advise and then the Executive Officers could equally ignore them and then the UK Biobank Officers would contract to the RCCs to deliver whatever they want to deliver, so it's a supplier customer role, which is completely foreign and in fact for the academics it was to them insulting [0102; p. 132; p. 3].

Spoke members described the hub as seeking consultation with the spokes but not heeding it; they therefore questioned the validity of seeking consultation and involving spokes at all in decision making. For example, a spoke member remarked: 'you can't have it both ways, so you can't want to run it through the universities and

then say ‘but we’re not going to listen to what you’ve got to say’ that simply doesn’t make any sense’ [0800; p. 193; p. 2].

Spoke members’ criticisms of the centralised model are strongly reflected in the documents pertaining to the process of contract negotiation, specifically in the spokes’ responses to the draft contract, emailed to representatives of the funding bodies on the 30 April 2004 [D550/10 Volume 1]. The responses detail the spokes’ discomfort at the control of the hub over the spokes in the draft contract; one response stated:

‘[t]he current draft reflects a project that is driven from the centre ... some aspects of Biobank should be centralised (centralised IT, centralised biorepository, etc), the RCCs cannot play their full role in Biobank if they are put in the position of having aspects of the project imposed upon them during the course of the project’ [their emphasis] [D550/10 Volume 1; p. 41].

Similarly, a further response referred to the ‘feel’ of the document and challenged the funders to ‘[c]ount up how many clauses are there to pin the RCCs down and then count the number that act in the opposite direction’ [D550/10 Volume 1; p. 41]. There is also evidence in the documents of the increasing awareness on the part of the funding bodies of the spokes’ criticism regarding the power granted to the hub. For example, a memo from a representative of the funding bodies to other representatives of the funding bodies on the 2 April 2004 explained the changes made to the terminology of the contract. For example, ‘[t]he document is now described as a Research Services Agreement and refers to the collaborative nature of the relationship between UK Biobank Limited and the RCCs’ [D550/10 Volume 1; p. 41].

Spoke members’ criticism of the role undertaken by the hub reflected their disapproval of the hub and spoke model as representing an attempted compromise between the academic scientific model and the business model. They felt the hub’s control over the spokes represented control by the business community over the academic scientific community. For example, a spoke member commented:

The culture that was with UK Biobank by having a Chief Executive Officer and Executive Officers is they took the view that they were running the whole project basically because it’s in their job descriptions and they were therefore looking at the RCCs ... in two roles: one is advisory and the second in a role of contractors or suppliers [0102; p. 132; p. 3].

Similarly, a spoke member referred to ‘far too much central control all along from a group of people who I think probably could not be expected to fully understand the scientific and university perspective’ [0800; p. 193; p. 2].

## 5.6 Organisational Changes

**‘It’s one person at Oxford that does the job’ [E2001; p. 6; p. 3]**

All constituent groups of interviewees interpreted the organisational changes as resolving the confusion over control of UK Biobank but they viewed it differently. For example, although academic scientists felt that the changes resolved the confusion they argued that as they were orchestrated by the funding bodies they reinforced their control over UK Biobank.

### 5.6.1 Organisational changes as resolution to confusion over control

All constituent groups of interviewees supported the move towards leadership by an individual, the new CEO *and* PI Rory Collins, from leadership by committee but supported it differently.

Academic scientists, particularly spoke members, stressed the powerful position adopted by Rory Collins, whereas representatives of the funding bodies and UK Biobank Limited refrained from such descriptions. For example, a spoke member commented: ‘Rory told the scientific leads this is how it’s going to be ... Rory decides the scientific issues and how they’re implemented and the scientific leads of RCCs support or don’t support them but he has the final say’ [E2001; p. 4; p. 8]. He continued: ‘it’s one person at Oxford that does the job’ [E2001; p. 6; p. 3]. Similarly another spoke member stated: ‘He is taking the control away from the PIs, the six coordinators and anyone involved in the study to Oxford’ [E2002; p. 8; p. 1]. Spoke members’ support for the institution of a leader was tempered by their criticism of the process of change. They were frustrated by how their role had suddenly transformed following years of effort to implement their former role. Despite these frustrations, some spoke members continued to support leadership by an individual. For example, a spoke member commented:

Perhaps the CEO taking responsibility, control, charge, whatever you want to call it is no bad thing as previously decisions were taking far too long. His new approach is ‘there is a job to do and he is the man to do it’ whereas previously there was much debate and revisiting of issues now there is much more control, sometimes decisions are taken with the involvement of the RCCs and sometimes not [E2002; p. 9; p. 2].

Their experience of the 'leadership by committee' approach, particularly the difficulty of appeasing committee members' multiple and vested interests, strengthened their belief in the institution of a leader:

I am coming round to it as previously there was so much petty politics involved in some universities and some people were squabbling like children so I suppose if we can't make up our minds and act appropriately then perhaps we need someone with a bit of authority and responsibility to do it for us [E2002; p. 9; p. 2].

Despite asserting their support for leadership by an individual in the organisational changes, representatives of the funding bodies cautiously criticised the former leadership by committee approach. For example, a representative of the funding bodies commented:

We've gone from a situation where we had a very consensual kind of committee approach which in a sense there was a bit of a leadership vacuum if I can even put it that way without being pejorative compared to having a Principal Investigator approach with somebody with very strong ideas on directing and leading the project [E2003; p. 11; p. 1].

This caution reflects their former defence of the leadership by committee approach and criticism of leadership by an individual in the original interviews. He continued:

I'm always a great believer and I think most people are in strong leadership ... I suppose you could say equally strong leaders can create waves but in my estimation what has happened over the last sort of six months there haven't been waves created and all of the stakeholder involvement and buy-in is all there and there's a great sense of confidence around the project [E2003; p. 11; p. 3].

Representatives of UK Biobank Limited articulated the changes as the adoption of a centralised approach. However, they cautiously associated a centralised approach with resolution to the confusion over control, which is indicative of the tension in the former hub and spoke model. For example, a representative of UK Biobank Limited commented:

We have a structure which allows us to better deliver the project in terms of cost and quality, I don't want to give you the impression that I'm some kind of Stalinist, centralist kind of person, everything must be run from the centre but

there are certain types of operation which are best run in a centralised, standardised way and those kinds of operation are those which are generally repeated processes, which is what we're doing that require a high degree of quality control and generate a lot of data which needs to be captured and processed and stored in a standardised way [E2006; p. 23; p. 2].

### 5.6.2 Motivation for the organisational changes

Academic scientists and representatives of the funding bodies and UK Biobank Limited also gave different accounts of the motivations behind the changes. Academic scientists implicated the funding bodies in the changes by holding them accountable for the failure of the hub and spoke model, prompting the need for change. They argued that the funding bodies' control of UK Biobank in the original structure was reflected in the difficulty of influencing the set up. For example, a clinical academic involved in UK Biobank associated the Wellcome Trust particularly in the failings of the original structure:

It was run, driven very heavily from within the Wellcome Trust, where there is not a good culture of thinking through the best way of doing something like this...the Wellcome Trust's a huge and very rich organisation and it's a very brave person who says "dear Wellcome Trust, you lay beautiful golden eggs but the goose that lays the golden eggs may actually not be laying them all in exactly the right places" or "the eggs are the wrong shape" and so on. It's very difficult for anyone to be critical of an organisation of the nature of the Wellcome Trust [E2010; p. 30; p. 3].

Similarly, a spoke member explained why he thought the hub and spoke model failed: 'most importantly a combination of not allowing sufficient autonomy within the regional collaborating centres and changing the rules' [E2005; p. 19; p. 2]. He pointed to the control exercised by the hub over the spokes:

Instead of asking for the principal investigators to contribute to the model for managing the trial...they [the funding bodies] imposed a model of management which actually was not going to work and they refused to allow us to modify that or to take ownership of it [E2005; p. 19; p. 2].

Academic scientists further interpreted the changes as representing the funding bodies' control over UK Biobank by arguing that the funding bodies appointed Rory Collins fully aware of the changes that he would implement. For example, a spoke member reflected: 'they knew that this is how Rory would do things...I would suspect it's the funders that drove the desire to have something done about the project' [E2001; p. 4; p. 9].

In contrast, representatives of funding bodies and UK Biobank Limited cited the changing requirements of the resource as motivating the need for change, specifically a greater control over UK Biobank by an individual. They argued that the implementation stage of UK Biobank required greater control of the hub over UK Biobank, whereas the earlier, developmental stage required consultation. In doing so, they justified their former support for the leadership by committee approach associated with the original organisational structure. For example, a representative of the funding bodies commented:

One was the phase of development of Biobank, I mean it was changing from the development of the protocol to piloting the study, so it was moving from a period of preparation, if you like, both sort of structural preparation and scientific preparation into the beginning of implementation. So the real changes were triggered by the needs of the project and that included the need to appoint a new CEO with John stepping down [E2011; p. 34; p. 5]

Similarly, a representative of UK Biobank Limited remarked:

In the early phases you do need a consultative approach, where you consult with the scientists across a very broad range of expertise to get their views on what could be done ... and then you try and boil that down into what should be done [E2006; p. 24; p. 3].



## 5.7 Conclusion

All constituent groups cited the following factors as being responsible for the alleged confusion over control of UK Biobank: lack of a leader, adoption of ‘leadership by committee’ as opposed to leadership by an individual, adoption of managerial leadership, adoption of scientific leadership, organisational structure, and lack of clarity regarding the role of the hub and spokes. Academic scientists speculated that control over UK Biobank lay with the funding bodies, which the funding bodies denied, which exacerbated the issue of confusion over control as academic scientists perceived such an active funding body role as contrary to standard academic scientific practice. Academic scientists further stressed the funding bodies’ control over UK Biobank by holding them responsible for orchestrating the organisational changes.

Academic scientists argued that the involvement of influential scientists and representatives of the funding bodies in the EWG, PDC, Science Committee and spokes resulted in confusion over control as representatives from each of these groups vied for position. They pointed to the difficulty of decision making as these groups advocated for their own scientific interests or that of their respective organisations, be it a university or a funding body. Representatives of the funding bodies argued that they had to involve numerous and large committees and groups as UK Biobank was a national initiative that would recruit across the UK. Some academic scientists accused the funding bodies of consulting so widely in order to be *seen* to be fair and avert criticism rather than any actual wish to consult them, which echoes PDC members’ criticism of consultation as not genuine. Some academic scientists felt that the multiple and vested interests arose out of the scientific design of UK Biobank. They argued that the lack of hypotheses meant that academic scientists competed to design the protocol in such a way to address their specific interests.

All constituent groups of interviewees interpreted the organisational changes, specifically the appointment of Rory Collins as PI *and* CEO, as resolving the confusion over control. They associated control of UK Biobank with leadership by an individual but they did so differently. Representatives of the funding bodies and UK Biobank Limited interpreted the organisational changes as resolving the confusion over control as they represented adoption of a centralised approach. They defined a

centralised approach as strong leadership and a powerful hub and associated it with business practice. Academic scientists did not interpret the adoption of a centralised approach as resolving confusion over control. This reflects the tension in the former hub and spoke model as spoke members resented the hub's control over the spokes, which they interpreted as rejection of academic scientific practice in favour of business practice.

## **Chapter 6**

**‘The funders developed a ‘them and us’ [academic scientists]mentality’ [030; p. 43; p. 4]**

### **Emergent Issues: Trust**

#### **6.1 Introduction**

Issues of trust, or lack of it, arose throughout the origins and development of UK Biobank. All constituent groups described a lack of trust between academic scientists on the one hand, and representatives of the funding bodies and UK Biobank Limited on the other. Representatives of the funding bodies and UK Biobank Limited did not trust academic scientists to develop UK Biobank as they questioned their motivations for becoming involved. Academic scientists felt that the funding bodies and UK Biobank Limited did not trust them to develop the resource citing the consultation process and organisational structure as evidence. In turn, they could not then trust the funding bodies and UK Biobank Limited. Whatever trust had existed between academic scientists and the funding bodies and UK Biobank Limited was tested by initial protocol development and gradually eroded through ongoing protocol development, the hub and spoke bidding process, contract negotiation, and implementation of the organisational changes.

This chapter will explore explanations for the lack of trust between academic scientists and representatives of the funding bodies and UK Biobank Limited. In doing so, it will focus on the following events and issues chronologically: protocol development, spoke members’ motivations for involvement, organisational structure and organisational changes. First, it will address academic scientists’ perceptions of the consultation undertaken in protocol development as evidence of the funding bodies and UK Biobank Limited’s lack of trust in them. Second, this chapter will examine spoke members’ motivations for becoming involved in UK Biobank, which partly accounted for the funding bodies and UK Biobank Limited’s lack of trust toward them. Third, it will analyse the influence of confusion within the

organisational structure as a source of mistrust and last, perceptions of the implementation of the organisational structure as responsible for a lack of trust.

## 6.2 Protocol Development

**‘whatever consultation there was, was basically justifying the decision post hoc’ [0900; p. 196; p. 2]**

Academic scientists argued that the funding bodies did not trust them with *initial* protocol development prior to the funding decision and *ongoing* protocol development following the funding decision. They cited an alleged lack of genuine consultation with academic scientists in protocol development as evidence of the lack of trust.

### 6.2.1 Initial and Ongoing protocol development

Academic scientists criticised the consultation undertaken with the PDC in initial protocol development. They argued that the Committee was not adequately consulted partly because of the projected timing of the funding decision. For example, a member of the PDC remarked:

because a decision has to be taken by April to, I mean, the idea that the whole thing was going to go live from April 2003 basically there was no time to change anything...you can talk about institutional sleepwalking or you can talk about railroading and you can talk about whatever you like but this was not in my mind the right way to develop a proposal which is probably going to cost over [£] 100 million in the end [051; p. 83; p. 8].

As discussed in previous chapters, academic scientists accused the funding bodies of having a pre-protocol in place prior to the establishment of the PDC. PDC members referred to the funding bodies’ role in the Committee as evidence of an alleged lack of genuine consultation. For example, the PDC member continued:

[we were] being told actually what the protocol should be because it was the same as the outline, and being told that any embellishment, even if it was cost-neutral in favour of an IPC was out of court or at least had to be justified as separate [051; p. 82; p. 8].

Some academic scientists referred to the Parliamentary Select Committee Report to support their criticism of the consultation process, specifically that the decision to go ahead with Biobank was made prior to consultation. For example, a member of the scientific community outwith UK Biobank commented:

The parliamentary select committee put it very well when they said that they got the impression that essentially they’d [the funding bodies] decided to do it

and whatever consultation there was, was basically justifying the decision post hoc [0900; p. 196; p. 2].

Academic scientists associated the alleged way in which the funding decision was taken, regardless of input from them, with their perception that the funding bodies did not trust them. For example, the scientist outwith UK Biobank continued:

There was a proposal put up behind closed doors, a decision made and then everybody basically saying “you do think this is a good idea don’t you?” ... nobody that was in the country dared say no because they all want funding from the MRC’ [0900; p. 196; p. 12].

They accused the funding bodies’ of wanting to be *seen* to involve academic scientists, rather than actually involving them. For example, 0900 commented:

You have to appear to be collegiate. If you’re putting that amount of money into medical research basically you have to give everybody their shout and I guess that was what that process was about, more about sort of making people *feel* they had some sort of shout in it [his emphasis] [0900; p. 196; p. 8].

Academic scientists argued that the wider academic scientific community outwith the PDC were not properly consulted. They accused the funding bodies of failing to heed critical academic scientists’ concerns. For example, a member of the PDC commented:

The Protocol Development Committee should have gone out of its way to attempt to reassure the people who were totally against it that their views were being taken into account...even if they’re not able to dissuade them they should have been doing all they possibly could to take on board the various comments of the people in the middle group, so the people with mixed views were listened to and frankly that didn’t happen [033; p. 51; p. 5].

Academic scientists criticised the Protocol Development Workshop and felt that it did not constitute genuine consultation. For example, the PDC member continued: ‘it allowed people to vent temporarily...it never really started a proper consultative process’ [033; p. 51; p. 5]. He reflected on the consequences of lack of consultation: ‘quite a lot of people have maintained that their views are being ignored and of course now it’s very hard to include people’s views because it’s so far down the design process’ [033; p. 51; p. 5].

Spoke members in particular cited what they felt to be a lack of genuine consultation with them in ongoing protocol development as evidence of the funding bodies' alleged lack of trust in academic scientists. For example, one spoke member remarked:

We've put together fairly detailed proposals for recruitment or for data collection or for questionnaire design or whatever...a lot of these proposals have largely been ignored ... the central people or what do you call them, Biobank Central or whatever, I think that my impression is that they have tended to go their own way despite the arguments that have been put to them and discussions that have been available [021; p. 21; p. 3-4].

They felt that their opinions were not acknowledged by UK Biobank Limited. For example, another spoke member commented that

having sought it [university involvement] very scant attention was paid to the views of really quite highly qualified individuals who knew both about the science and about how to manage large research projects, and who were well aware of what would be needed in order to make involvement in such an enterprise worthwhile for the universities [0800; p. 193; p. 2].

Representatives of the funding bodies dismissed academic scientists' criticism of the consultation process as indicative of the academic scientists' suspicions of them. For example, a representative of the funding bodies commented:

Biobank has always been open...that's not necessarily the perspective given by some of the opponents to Biobank and it's biased from one perspective, they've always been sort of Machiavellian in their thinking assuming that there's been a lot of things going on behind closed doors to make decisions and that has never been the case...people do like to lift the curtain and try to find something there that isn't necessarily there [042; p. 64; p. 2].

Representatives of UK Biobank Limited distinguished between *initial* and *ongoing* protocol development. They were sympathetic to academic scientists' criticisms of the consultation involved in *initial* protocol development. For example, a representative of UK Biobank Limited reflected:

They discussed them [main issues] and I think ultimately Tom Meade just decided and that's okay but it wasn't ideal because we've been left with a legacy of people feeling that they never had that really proper evaluation, so to

some extent they were fudged in that the original protocol doesn't reject the interests of the intensively phenotyped cohort [010; p. 3; p. 5].

In relation to *ongoing* protocol development, representatives of UK Biobank Limited did however dismiss academic scientists' criticisms of the consultation process. They accused academic scientists of trying to change aspects of the protocol that had already been agreed. For example, the representative of UK Biobank Limited continued:

They're [spoke members] still trying to introduce that in by the back door (lower age range) which is very irritating and one of the problems we have is that people are still ... there's still a lot of entropy in the system, people have not fully signed up to the protocol, they've signed with their fingers crossed behind their back hoping that they can change it and it's not great [010; p. 3; p. 5].

#### 6.2.2 Development of IPC Protocol

Members of the PDC described the development of the IPC protocol as illustrative of the funding bodies' lack of trust in them. The IPC was a highly controversial issue and a PDC member said the funding bodies' decision not to include the IPC in the main protocol was 'from a scientific perspective I personally think this is the biggest single error that Biobank has made' [033; p. 50; p. 7]. Members of the PDC accused the funding bodies of not allowing them to genuinely consider the IPC. For example, the member of the PDC continued:

Discussion took place on that but it was very much..., it was never allowed to get to the point where it was seriously going to become part of the project so they allowed us to discuss it but in a fairly safe manner which wasn't going to allow us to get what we wanted [033; p. 50; p. 7].

They argued that the funding bodies' negative reaction to the IPC proposal reflected a lack of trust in the PDC, rather than any particular objections to the IPC. For example, another member of the PDC felt that the IPC was 'inevitably perceived as a threat, by whom? Difficult to say at this stage, but clearly the chairman, Tom Meade, saw this as something which should be set on one side' [051; p. 83; p. 6]. He continued by describing the effect of such lack of trust on the Committee:



A lot of ideas that came from the Protocol Development Committee actually went into the IPC proposal rather than into the main protocol because that was where we perceived efficiency and scientific gain ... it did emancipate the Protocol Development Committee to basically say, well, its allegiance lay more with the IPC idea than with a hand-me-down Biobank protocol [051; p. 83; p. 9].

Documentary evidence of the funding bodies' alleged lack of trust of the PDC in developing the IPC protocol includes correspondence between members. PDC members described efforts taken to present the IPC protocol as non-threatening to the main protocol, which is indicative of the tension between them and representatives of the funding bodies. For example, a member of the PDC, in an email to the Committee on the 17 November 2001, refuted accusations made by the funding bodies that the IPC sub-group 'have some vested interest' in the main protocol failing as 'frankly ridiculous' [S600/174; Volume 2; p. 19]. He criticised the funding bodies' lack of trust of the IPC sub-group by describing how the IPC relied on the success of the main protocol. He pointed out that members of the sub-group were involved in spoke bids despite expecting that the IPC would not be funded as part of the main initiative, arguing 'these hardly sound like the rational actions of a group of subversives hell bent on the downfall of the main initiative' [S600/174; Volume 2; p. 19]. Lack of trust between PDC members and the funding bodies is further evident in an email from another member of the PDC. In a letter to Tom Meade, copied to members of the Committee, on the 16 November 2001, he questioned the basis of the decision that the IPC protocol would be sent to the peer review panel in a revised form:

Who was present at the meeting which took this decision? ...who will take the decision about whether this revised document is 'suitable' for peer review? ...whom did this group represent (the PDC, all funders, MRC only, or none of these? ...what steps have been taken to elicit views of those not represented at this meeting? ...will the fuller IPC protocol be made available to peer reviewers on request? [S600/174; Volume 2; p. 20].

### 6.3 Spoke members' motivations for involvement

**'There was a bit of "what's in it for me?" mantra sitting behind a number of people' [043; p. 70; p. 15]**

Academic scientists and representatives of the funding bodies and UK Biobank Limited had different understandings of spokes members' motivations for involvement in UK Biobank. On the one hand, academic scientists pointed to their professional obligations to their universities in taking part in research activities in terms of the Research Assessment Exercise (RAE). On the other hand, representatives of the funding bodies and UK Biobank Limited criticised such 'non-scientific' motivations. These different understandings regarding the validity of 'non-scientific' motivations for involvement contributed to a lack of trust between academic scientists and representatives of the funding bodies and UK Biobank Limited.

#### 6.3.1 Spoke members' motivations for involvement

Spoke members articulated their motivations for involvement in the following terms: the desire simply to be involved in a large scale, national initiative; the professional and financial risks of not being involved; and the potential for collaboration with other universities. Generally, they did not describe scientific interest or belief in the value of UK Biobank as a significant motivating factor.

Spoke members felt that they *should* be involved in UK Biobank and described such pressure as a significant motivating factor in applying to be a spoke. For example, a spoke member stated: 'we were better having a spoke than not having a spoke, we're better contributing intellectually than not, we're better in the party than out, than writing from the sidelines' [026; p. 38; p. 3]. Similarly, another spoke member reflected on the fear of being left out of 'one of the largest epidemiological projects happening in the UK over the next ten years' and a certain 'anxiety of being in some way left out of the biggest show in town' [0105; p. 140; p. 3].

Spoke members feared being professionally and financially isolated if they were not involved in UK Biobank. For example, a spoke member commented: 'there was an opportunity cost if we weren't involved would we be a player or not?...we set ourselves up to be one of the top departments...if we weren't involved in this how

might we be perceived?’ [023; p. 28; p. 2]. They feared that their university departments would face financial difficulties in the future if they were not involved in UK Biobank. For example, a spoke member remarked:

A large amount of biomedical research funding might essentially be tied up in Biobank over the next few years because it was such an expensive project...if you wanted to access biomedical research funding it was probably strategically sensible to in some way be part of Biobank [0105; p. 140; p. 3].

Spoke members argued that the funding of UK Biobank would negatively affect the available funding for other medical research activities and thus felt that it was crucial to be involved in order to access the available funds. For example, a spoke member reflected:

There is a finite amount of money in the UK for medical research of the epidemiological type so there is a fear that all the money is going to one project there won’t be much for other projects, so you’d better apply for the money that’s available ... people don’t want to not be in it if it’s going to be the major medical research in Britain for the next fifteen years, it’s nice to be in it, not out of it [0501; p. 174; p. 2].

Similarly, a scientist outwith UK Biobank [0302] remarked:

It was a major epidemiological study that would be consuming a lot of resources, the sort of things that ideally one needed to be on the inside rather than the outside in order to get access to both the resources and ultimately to the scientific spin-off [0302; p. 163; p. 4].

Despite doubts over the issue of payback for involvement (addressed in the next section), spoke members maintained their wish to stay involved in UK Biobank, such was their fear of the professional and financial consequences of not being a part of it. For example, a spoke member stated: ‘you might benefit from it and in the long term if there is an increased investment in this and that you’ll certainly be out in the cold if you’re not in at the beginning’ [052; p. 89; p. 7].

Spoke members cited the potential for collaboration between universities as a further motivating factor, which was also irrespective of their belief in the initiative. For example, a spoke member remarked that ‘it would cement some of the earlier initiatives that we’d set up on research in primary care ... it’s a way of interacting and working with secondary care colleagues as well’ [023; p. 28; p. 3]. Similarly, another

spoke member described involvement in UK Biobank as ‘a nice catalyst for developing that collaboration’ [0201; p. 148; p. 6]. Spoke members acknowledged the ‘non-scientific’ nature of these motivations. They argued that ‘non-scientific’ motivators were typical of standard academic scientific practice. For example, a spoke member reflected:

Our interest was always ulterior. It wasn’t in the study in itself, it was in the potential acquisition of research infrastructure which would have value for other things...it was also recognised as being an opportunity to collaborate more effectively with hospital colleagues ... if there weren’t ulterior purposes then why would anybody get involved in a study, never mind the uncertainties as to the resourcing of it [022; p. 26; p. 4].

There was, however, an exception; one spoke member voiced the motivations for involvement in distinctly different terms. He did not consider the professional advantages of involvement important and focused on the value of a contractual relationship as that of a service provider. He distinguished between involvement in UK Biobank and designing and implementing personal research activities. For example, he commented: ‘this is like contracting. This isn’t like what we do for our *research* research...this isn’t a study I designed, this is a study someone wants to do and we are professionals at getting people through the doors [his emphasis]’ [0204; p. 156; p. 4]. However he appeared to be expecting a financial payback for involvement as a spoke whereas other spoke members did not envisage such a return, which may partly account for the different perspective. For example, he continued:

It’s forty million pounds, better to be in than out...given that someone’s throwing forty million at it ... I’ve got hungry mouths to feed...I’ve got a big research unit here and if it keeps us here and in work that’s great, good contract research [0204; p. 156; p. 2].

### 6.3.2 Criticisms of spokes members’ motivations for involvement

Representatives of the funding bodies and UK Biobank Limited doubted academic scientists’ commitment to UK Biobank feeling that spokes had ‘non-scientific’ motivations, which fuelled mistrust. For example, a representative of UK Biobank Limited remarked:

The problem with Biobank is it's such a big project that people don't want to say "well, it isn't quite what I wanted it to be therefore I'm not going to be involved". They (academic scientists) felt they had to be involved, they had to try to get involved anyway because it was such a big project, so they've been brought into it against their will, with a sort of feeling "well, I'm going to have to do this" which is unfortunate [010; p. 3; p. 6].

They felt that spoke members were less interested in the success of the resource and more interested in the value of involvement to their respective universities. For example, despite acknowledging the pressures on the academic scientific community ('it's in this modern age of RAE's and all the rest of it and the kind of pressures that universities are under, having to go back to their own universities and justify their participation' [043; p. 70; p. 15]) a representative of the funding bodies stated:

There was a bit of "what's in it for me?" mantra sitting behind a number of people...I think that led to some confusion in people's minds as to if they did participate in Biobank, what did it mean to them individually rather than thinking that they're just contributing to a national resource [043; p. 70; p. 15].

Similarly, another representative of the funding bodies commented: 'the scientific community did not want it established that way, I mean, they wanted, some of them wanted little playgrounds that they could go and do their own little projects in' [063; p. 67; p. 15]. Academic scientists criticised the funding bodies and UK Biobank Limited for failing to understand spoke members' professional responsibilities to their universities in taking part in UK Biobank.

## 6.4 Organisational Structure

**‘we were getting conflicting messages “we want your scientists and you driving the research agenda but we don’t really want you doing that because you’ve got to work to a central protocol that you can’t add to” [023; p. 30; p. 4]**

The policy that spokes would not get any preferential access to the data or samples contributed to academic scientists’ lack of trust towards the funding bodies and UK Biobank Limited. Academic scientists criticised the funding bodies and UK Biobank Limited for the lack of understanding the policy showed of their professional obligations in becoming involved in UK Biobank. The issue of preferential access for academic scientists involved in UK Biobank is part of a wider debate regarding open access to datasets. The two main funding bodies, the MRC and the Wellcome Trust, have worked in parallel towards open access for all datasets for a number of years. For example, both funding bodies were involved in securing open access to the human genome sequence in the HGP. Confusion surrounding the policy on spoke access further contributed to the lack of trust between academic scientists and representatives of the funding bodies and UK Biobank Limited. Academic scientists were also confused about the following aspects of the organisational structure: the bidding process, the role of the spokes and the nature of UK Biobank Limited. They attributed their lack of trust of the funding bodies and UK Biobank Limited to an alleged lack of clarity surrounding these organisational issues.

### 6.4.1 Lack of spoke payback

Academic scientists argued that some form of payback, financial or intellectual through preferential access to the resource, was a condition of their involvement in UK Biobank as spoke members. They described how they had to justify their participation to the academic institutions they were employed by and that without any reward, financial or intellectual, their position was untenable. For example, a spoke member stated that ‘two kinds of payback are either financial for the universities or institutions and academic access to the data so that we can get publications and research benefits ourselves’ [021; p. 21; p. 2]. Spoke members felt that the lack of preferential access was unfair, as it meant that academic scientists who were not

involved in developing the protocol or recruitment would have the same rights of access as academic scientists who were involved. For example, a spoke member complained that they would have to

compete with others, possibly in the United States, who have not been involved and so there are tensions...it is difficult for academics as they think in publications and they put in a lot of time and thought on it and then you may have some Harvard person getting access and you would be very frustrated I think [035; p. 56; p. 9].

They argued that the lack of preferential access would mean that they would be contributing to other academic scientists' publication records and other universities' inputs to the RAEs, rather than their own. For example, another spoke member reflected:

It (UK Biobank) would be a great deal better if it involved academics who were investigators, drawing on the data and getting publications out of it as it would then justify the time, so that instead of doing the work for other people's publications we were working on our own [0101; p. 130; p. 3].

Academic scientists further criticised the policy in terms of its effect on spokes' role in UK Biobank. For example, a member of the EWG continued: 'it [lack of spoke payback] really turns the regional coordinating centres into sort of stamp collectors' [060; p. 91; p. 3]. Spoke members' frustration regarding the funding bodies' apparent lack of understanding of their requirements fuelled their mistrust. They resented their involvement in the resource given the lack of payback. For example, a spoke member commented:

We are taking a day out when we could be writing our own research proposals, writing another paper, and papers from this project will not be coming out for at least five years. In the meantime there is that opportunity cost to us of intellectual and physical energy being directed into a project that might actually have minimal output for an individual or an individual's institution [023; p. 30; p. 6].

Spoke members explained how the policy had made them question the worth of continued involvement in UK Biobank. For example, a spoke member remarked:

From their [spokes] perspective they're subsidising UK Biobank and the only other thing that universities want is academic kudos, and because of the

intellectual property rights and access policy the stance of the funders has been “this is open access” so I know that many universities are questioning “well, why take part” [0102; p. 133; p. 3].

Similarly, another spoke member stated: ‘the model depends on academics like myself and we have to justify the time, given that we are not gaining anything towards the RAE so there is a risk of people pulling out, which is a high risk’ [0101; p. 130; p. 2]. Spoke members strongly associated the policy with the potential withdrawal of universities from the resource. For example, another spoke member commented:

There’s a lot of suspicion from the universities, you know, very, very high level suspicion as to whether it’s still worth being involved in a UK Biobank. I think it’s true as to now because it’s not clear what the research credits to the universities are...frankly, it’s high risk [0104; p. 138; p. 2].

A further spoke member concurred:

If you’re going to do some science, you want to actually get something out of it and publish some papers and so on but if it’s something that you in particular aren’t going to benefit from then you think “well, why am I getting involved with it?” [052; p. 89; p. 7].

Academic scientists further attributed their lack of trust of the funding bodies and UK Biobank Limited to the policy as it rendered involvement in UK Biobank a risk. They pointed to the direct financial costs of being a spoke and the potential cost of missed research opportunities because of involvement in UK Biobank. For example, a member of the PDC commented:

There’s very, very mixed feelings about whether this is really of any benefit to the people who are taking it on, and of course it’s a substantial opportunity cost if you want to do it properly...those people who got Biobank spokes must be thinking three times over about “is this going to cover full economic costs?” [051; p. 86; p. 12].

Given the apparent lack of any payback, academic scientists felt that any potential benefits of being a spoke were not proportional to the risk involved. For example, a member of the EWG remarked:

If by doing it, you don’t have time to do much else but you don’t actually get to analyse the data and test your hypothesis, then there’s no carrot ... if the academic leadership doesn’t get any rewards, then the way that the universities



are judged and academic success is judged is that you can't commit to. It'd be academic suicide' [062; p. 103; p. 14].

Spoke members, in particular, interpreted the signing of a contract with the hub as financially riskier than receiving a grant. They also criticised the idea of a contract as they felt it represented an unequal relationship between the spokes and the hub, whereby control lay with the hub. For example, a spoke member stated:

UK Biobank would like to have one formal contract but I think the universities are still saying "You don't give us enough money to take risks therefore we want a grant" ... you give it [a grant] to the university on the basis that they will deliver the project they've just said they will deliver. It's a different relationship because it means that you have a more equal relationship between the grant provider and the grant receiver, in that there will be a more equal negotiation if the project doesn't deliver what it's initially thought they could negotiate as to what direction it could take as an alternative but the grant doesn't suddenly get pulled away, it has been given [0102; p. 133; p. 4].

This criticism reflects academic scientists' perceptions of the establishment of the hub as a company as representing business, as opposed to academic scientific, practice.

Some academic scientists criticised the necessity for financial or intellectual reward for their involvement in research activities. They lamented that scientific interest alone was not enough motivation for academic scientists to become involved in research, yet conceded that this was the reality. For example, a member of the EWG commented:

It's unfortunate, these days one of the motivations for taking part in a study almost regardless of whether it attracts you or not is money. It's so important for people now to be seen to be raising funds for their departments and universities that the sort of scientific interest sometimes seems to take second, back seat [060; p. 91; p. 3].

Representatives of the funding bodies and UK Biobank Limited acknowledged academic scientists' arguments regarding the importance of financial or intellectual payback, but downplayed them. Given that they perceived the spokes' role solely in terms of recruitment, they questioned the extent to which spokes deserved payback,

particularly intellectually through preferential access. For example, a representative of UK Biobank Limited reflected:

The deal on offer to the RCCs is essentially unattractive to them and I'm sure people have said that and I agree ... they are not the only people who could do Biobank, we could manage without them. It'd be a public relations problem if everyone dropped out but essentially what we need the RCC's for is to set up clinics and help us recruit people but that isn't difficult [010; p. 7; p. 17].

Representatives of the funding bodies and UK Biobank Limited rejected spoke members' assertions that their role also involved protocol development, and hence reiterated that spokes did not warrant preferential access to the resource. For example, the representative of UK Biobank Limited continued:

They are arguing that they are putting in their intellectual input into Biobank and they need intellectual pay-off but the fact is they're not putting intellectual input into it because they're not delivering ... most of the intellectual input was already in the protocol...lots of people are contributing, not just the RCCs and I don't think they have a very strong argument that they should have access to the data [010; p. 7; p. 17].

#### 6.4.2 Confusion regarding spoke payback policy

Academic scientists partly attributed their lack of trust of the funding bodies and UK Biobank Limited to a lack of consistency regarding the policy on spoke payback. They argued that it was not clear whether or not spoke members would be granted preferential access. For example, a spoke member commented: 'there was a lot of dilly-dallying and people not really wanting to say either way whether there would be access' [0203; p. 152; p. 3]. Similarly, another spoke member remarked how there was no 'explicit statement saying you will not be able to see data in advance or exclusive' [0102; p. 134; p. 8].

On the one hand, some academic scientists argued that it was generally understood that access would be granted. They acknowledged the lack of formal documentation regarding the policy yet maintained how, prior to hub and spoke selection, it was generally accepted. For example, a member of the EWG stated:

It was always very clearly understood and nobody ever contradicted this that the spokes...would have a certain amount of opportunity to do their own thing, you know, follow their own particular interests and I think that involved, obviously, and would have involved retaining some of the data that they had collected' [060; p. 91; p. 2].

The EWG member continued:

There's no doubt that whether it was recorded or not it was firmly understood beforehand that there would be this degree of freedom over enabling regional coordinating centres to collect additional samples, for example, of the things they might want to do and to have some of the data [060; p. 92; p. 3].

Academic scientists argued that a lack of clarity surrounding spoke payback was indicative of confusion regarding the development of UK Biobank generally. They associated this confusion with an alleged lack of control of the resource. For example, a member of the EWG commented: 'They've not been able to resolve exactly who was running this project and who was benefiting, who was going to get what out of it' [061; p. 96; p. 9]. On the other hand, representatives of the funding bodies and UK Biobank Limited argued that it was explicit that preferential access would not be granted. For example, a representative of UK Biobank Limited remarked:

They've always known that the funders set up Biobank as a resource with open access, that was always the idea. It was absolutely blindingly obvious to them that this is how it was done and they just didn't accept it...signing it with their fingers crossed [010; p. 7; p. 17].

Documentary evidence of a lack of consistency concerning spoke payback, and the issue of preferential access in particular, includes the minutes of the EWG meetings and the Final Report of the EWG. These documents suggest that spokes would be granted preferential access. For example, the notes from the second meeting of the EWG stated that each spoke 'could add supplementary components to the core according to their own interests' [S600/161 Volume 1; p. 7], a stance justified in the third meeting as allowing: 'increased richness of dataset, and greater involvement of local centres' [S600/161 Volume 1; p. 7]. These terms are further developed in the Final Report of the EWG which stated that 'researchers generating data could have an agreed period of preferential access before being required to place their data in the common dataset' [S600/161 Volume 2; p. 7].

### 6.4.3 Confusion over the bidding process

Spoke members criticised the allegedly confusing bidding process and suggested it led to their lack of trust in the funding bodies and UK Biobank Limited. They argued that the funding bodies did not make their requirements to the bidders clear, specifically whether or not it was necessary to detail scientific opinion or interest in the area. Spoke members remarked on how they were not required to detail their scientific opinion or interest. For example, a spoke member remarked:

The aspect that was most surprising when we did it [put in the spoke bid] was that actually there was no focus on their scientific interests, it was all about your experience of collecting DNA samples for epidemiological information but actually nothing about your perspective on the science [0103; p. 137; p. 11].

He continued: ‘there had been nowhere on the application form to talk about your science’ [0103; p. 137; p.13]. Spoke members identified this issue as a further source of confusion and one spoke member recalled how his spoke was criticised for having not detailed their scientific opinion or interest in the initiative. He commented:

One of the comments we got at our submission from George Radda was “there doesn’t seem to be much science in this”...we were getting conflicting messages “we want your scientists and you driving the research agenda but we don’t really want you doing that because you’ve got to work to a central protocol that you can’t add to” [023; p. 30; p. 4].

They also described confusion regarding the outcome of the bidding process, particularly regarding the role of the spokes and the financial arrangements between them and the hub. For example, a spoke member referred to a

lack of consistency and the moving of goalposts...you thought that you were doing one thing and then you discovered that you weren’t, we thought that you bid for a project and then you just get the “well actually, you’ve been selected” but it didn’t really mean that you’d got the funds or that you were being asked to do what you’d bid to do, so it has been very confusing [0800; p. 192; p. 3].

Academic scientists criticised the competitive and confidential nature of the bidding process and thought it contributed to the lack of trust between them and the funding bodies and UK Biobank Limited. They argued that such confidentiality was particularly unnecessary and unusual in the academic scientific community. For example, a member of the PDC reflected:

You would have got a better portfolio of spokes if people had discussed more openly with each other what they were proposing...the whole thing was channelled into a highly competitive mode from the very earliest declaration of interest stage and it got worse as you moved through the short listing to the detailed tender stage [051; p. 86; p. 10].

Academic scientists further criticised the competitive bidding process for reflecting business, rather than the academic scientific, practice. For example, the member of the PDC continued: ‘from an early stage in the proceedings those people who were compiling the bids were instructed not to discuss with other bidders, as if this was some sort of commercial contract with industrial espionage’ [051; p. 86; p. 10]. Similarly, a spoke member commented: ‘it was a New Labour thing, it’s almost like Trusts within the healthcare systems, you want to actually be very cooperative and yet they were setting it up that the Trusts compete with each other’ [0103; p. 137; p. 7]. Some spoke members argued that the secretive bidding process reflected a wider confusion over whether UK Biobank was an academic scientific or business endeavour. For example, a spoke member criticised the

excessive amount of bureaucracy and straitjacketing...we weren’t allowed to talk to others, which frankly in a developmental process is not very helpful...a lack of clarity it seemed to me about whether we were involved in a scientific endeavour or a commercial endeavour [0800; p. 192; p. 6].

Representatives of the funding bodies and UK Biobank Limited attributed the lack of clarity and confidential bidding process to the EU Procurement Rules process that it followed. For example, a representative of the funding bodies remarked:

There was a lot of feeling outside that it had been very longwinded, the bidding process had involved a lot of work and it seemed very bureaucratic but we were kind of stuck with it because of the EU procurement rules, we had legal advice to say that we should follow that particular path, so that’s what made our lives a lot more difficult [043; p.70; p. 13].

They felt that misunderstanding of this process accounted for a lack of trust as academic scientists did not realise that the process had to be confidential on account of these rules, rather than because the funding bodies wanted it that way. For example, another representative of the funding bodies stated:

There was an enormous rift I guess between the funders and the people that were bidding in to that whole process, be it the spokes or the hub in why you had to go through this hideous process of satisfying the European procurement rules [042; p. 66; p. 12].

Some academic scientists did however understand the process and nevertheless criticised the funding bodies for following EU Procurement Rules:

They went through a process of, enforced by things that are greater than any of us, to go through a process of contracting by European law which led them into a position where the funding model left the universities in a position where they could not claim this activity as a research activity, so it didn't count for RAE purposes' [061; p. 96; p. 9].

#### 6.4.4 Confusion over the role of spokes

All constituent groups attributed misunderstandings about the spokes' role in UK Biobank to the lack of trust between academic scientists (particularly spoke members) and representatives of the funding bodies and UK Biobank Limited. These misunderstandings concerned the extent to which spoke members would be involved in designing the protocol, specifically in forming the Standard Operating Procedures (SOPs) from which participants would join the resource. There were also differences in understandings of the extent to which spoke members could alter the SOPs to suit local populations. All constituent groups felt that if the proposed role of the spokes had been clear then there would not have been such a lack of trust. For example, a representative of the funding bodies remarked:

When the spokes had been selected there had been a very clear mandate that the object of the spoke is to go out and recruit 10,000 individuals in your particular geographical area, and you're going to do it in this way and collect that data, and you're going to collect it over this time period. If that mandate had been made totally clear you would have ended up with a different set of players now to what you've got and end up with something, an infrastructure,

that would be up and running today when we're still mucking around [063; p. 67; p. 15].

Spoke members criticised the implication that their role lay solely in recruiting individuals according to a protocol designed by UK Biobank Limited and the funding bodies. They felt that their involvement in initial and ongoing protocol development merited a more equal partnership with the funding bodies and UK Biobank Limited. For example, a spoke member stated:

We were going into this as research partners, to a certain extent since then it seems that the attempt has been made to reclass us as basically service providers ... if it's essentially just a simple service relationship whereby we get paid to provide x thousand participants and at the end of the day we're just told "thanks for providing those participants" then that's basically the relationship that primary care had in the old days with a lot of drug companies in terms of its involvement in the sort of research that they were involved in, that is not now the relationship that we're interested in having with the funders [0105; p. 142; p. 8].

They argued that a recruitment role was 'unacademic' and therefore inappropriate for academic scientists to undertake. For example, another spoke member commented: 'because we're academics, we do things for academic payoff...we're not recruitment organisations, we're not just recruiting for other people's work' [0200; p. 145; p. 11]. Similarly, a scientist outwith UK Biobank commented on how there was

very little of any academic interest in it for them...they're essentially running themselves as sort of commercial survey organisations and given you've got to do it like that, you might as well privatise the whole thing it seems to me [0900; p. 199; p. 13].

Spoke members' criticism of the proposed recruitment only role was exacerbated by the lack of any payback, particularly through preferential access to the resource, for their involvement. They stressed how this lack of payback was contrary to standard academic scientific practice. For example, a spoke member reflected:

We would service the hub by giving them 100,000 people and that's it – thanks very much for your help, which is not the way science generically in this country ever really works. It's always been collaborative, that you get something in return for delivering 100,000 people [0503; p. 178; p. 10].

Spoke members criticised the funding bodies for hindering their role and argued that the funding bodies treated spoke members' attempts to increase their involvement with suspicion. For example, a spoke member remarked:

The funders would not pass over the decision making, they were untrusting and felt that the RCCs had a hidden agenda when they set up the Implementation Group, which was a shame as the group was important. It was hindered because of their lack of trust and fears that we had a hidden agenda, the funders developed a 'them and us' mentality [030; p. 43; p. 4].

One spoke member adopted a highly unusual position regarding the role of spokes. He was not critical of the role and rather welcomed the opportunity to act as a service provider to UK Biobank Limited. For example, the spoke member explained: 'they're paying you money and you do a study for them, you know, it's that sort of thing. They want a hundred thousand people led and questioned, well, we can do it' [0204; p. 156; p. 2]. This spoke member was however referring to financial payback, which may explain his unusual stance as other spoke members were not expecting to receive any such return. Nevertheless he did not object to the role as being not being appropriate to academic scientists.

Documentary evidence of a lack of trust due to confusion surrounding spokes' role includes the process of contract negotiation following spoke selection. In their response to the draft contract between them and UK Biobank Limited (contained in emails from spoke representatives to funding body representatives on 30 April 2004), spoke members criticised the funding bodies for not providing enough information on the proposed role of spokes. For example, a response stated:

The current structure of the document leaves the RCCs exposed to a set of unquantifiable risks. For instance the RCCs are being asked to enter into a legally-binding obligation to deliver a set of deliverables that are not adequately defined [their emphasis] [D550/10 Volume 1; p. 40].

This alleged lack of clarity in the draft contract fuelled spoke members' suspicions of the funding bodies. For example, a response expressed concern that 'policies will be imposed upon us but we won't know their content at the time of signature of this agreement' [D550/10 Volume 1; p. 42]. A further response echoed this sentiment pertaining to 'concern that we won't know how much we will be paid until after the



contract is signed' [D550/10 Volume 1; p. 42]. Spoke members felt that the draft contract only recognised their role in recruitment and not their involvement in protocol development. For example, one response complained how

the wording of the draft contract gives the very clear impression that, rather than it being a mechanism for formally recognising the academic contribution made to the project by the RCCs...it is a hard-nosed tool for pinning the RCCs down to deliver a set of deliverables and which hardly recognise the other things that the RCCs are contributing...mainly because these are not being costed or paid for [D550/10 Volume 1; p. 42].

Similarly another response stressed that

the contribution of the RCCs to both the science behind Biobank and the delivery of the fieldwork must be recognised, as does the fact that the RCCs are an integral part of Biobank without which the overall project could not be delivered [D550/10 Volume 1; p. 41].

Spoke members criticised the proposed relationship between the hub and the spokes in the draft contract. For example, one response called for the contract to

‘reflect a rather different relationship between the RCCs and UK Biobank than is implied in the current document’ and called for them to be seen ‘more as partners (in the general sense of the word)...taking joint responsibility in delivering the project and sharing in its success’ [D550/10 Volume 1; p. 40].

Spoke members distanced themselves from the type of role they believed to be offered by the funding bodies. For example, a response pointed out:

This is still a contract for services (albeit called ‘research services’) and ‘the RCCs are not simply supplying a set of Research Services akin to those that could be purchased from a contract research house for example. They feel they can and are offering far more [D550/10 Volume 1; p. 41].

A further response described

a slight mismatch between the role the RCCs feel they are taking in the project and the role that appears to be being offered by Biobank. Quite naturally this mismatch has found its way into the draft contract and has therefore become a matter for attention [D550/10 Volume 1; p. 41].

This ‘mismatch’ in understanding of the role of spokes between spoke members and representatives of the funding bodies and UK Biobank Limited fuelled mistrust.

#### 6.4.5 Confusion over the nature of UK Biobank Limited

Spoke members also attributed the lack of trust between them and representatives of the funding bodies and UK Biobank Limited to confusion regarding the nature of UK Biobank Limited. They felt that the funding bodies did not make the nature of the hub clear, particularly the proposed relationship between it and the spokes. Spoke members argued that the funding bodies had ulterior motives in involving universities as spokes that did not concern recruitment. They pointed to the importance of securing future university involvement in UK Biobank, through accessing the database, to the success of the company. For example, a spoke member commented:

The first structure was a confusion of what is the UK Biobank Limited...the funders saw it as a company tasked with delivering a project and its survival and funding was a part of a business plan, so that they had to deliver a project and then had to find ways of generating income from that project to survive as an organisation, as a company, and the subtext of it would be that in order to do that it had to engage with universities across the country, so that the universities have a vested interest in making sure that funding is given to UK Biobank via other routes by the universities wanting to use the resource [E2001; p. 7; p. 7].

Spoke members argued that the funding bodies did not make the extent of their intentions clear when canvassing academic scientists' support, which they felt contributed to the confusion regarding the nature of UK Biobank Limited. They felt that the funding bodies involved universities in a business sense to enable the success of the company rather than in an academic sense to contribute to the success of the resource. For example, the spoke member continued:

The involvement of the other universities was partly required by the funders but also as part of a, as it were from my thinking, a longer term plan in engaging the academic community so that UK Biobank was sustainable in business terms, and so the role of the RCCs then became a business relationship, which upset the academics who thought that they were having a scientific relationship...you had parallel sets of communities working on both levels and neither being able to do much without the other, but neither culture

was willing to necessarily recognise that there was a need for compromise between the two [E2001; p. 7; p. 7].

## 6.5 Organisational Changes

**‘we [a spoke] felt very let down by the whole thing’ [E2007; p. 26; p. 6]**

Academic scientists attributed the lack of trust between themselves and representatives of the funding bodies and UK Biobank Limited to the way in which the organisational changes were implemented. They criticised the alleged lack of consultation regarding the changes, their timing and effect on spokes generally.

### 6.5.1 Implementation of organisational changes

Spoke members criticised the alleged lack of consultation regarding both the nature and implementation of the changes. For example, a spoke member remarked: ‘It was discussed at a Steering Group but it was a fait accompli and would have got the go-ahead regardless of what anyone else thought’ [E2002; p. 8; p. 1]. They felt that confusion regarding the nature of the changes contributed to their lack of trust of the funding bodies and UK Biobank Limited. For example, another spoke member commented:

It’s been a bit of a shambles...we’ve been given a small budget to run things and start things off the ground and that’s finished and we had recruited someone to help get this study running and their job went effectively, it was all terribly insecure ... one minute you’re being told one direction and the next minute you’re told to sort of do a u-turn and then do another u-turn after that, so for us it’s been I think quite unsettling...we felt very let down by the whole thing [E2007; p. 26; p. 6]

Spoke members argued that the changes were implemented too suddenly, which exacerbated the problems caused by an alleged lack of consultation regarding them. For example, E2002 continued:

There is a lack of consultation about the decisions being made. For example, we had a call centre contract about to be commissioned just days away from being completed and it was cancelled by Rory Collins, and the call centre function is now going to Oxford for the pilot and for the main study it is going to be the Welsh RCC...there was no consultation, no rationale why the development of a professional call centre was stopped and no explanation why it was moved to a university with no professional experience. It was all of a

sudden stopped and no reason was given...this example typifies the problem of a lack of consultation [E2002; p. 8; p. 3].

They felt that this timing hampered UK Biobank's reputation as a credible initiative, as the changes were made amidst planning for a forthcoming pilot study. For example, E2002 said:

Before he [Rory Collins] was appointed we were working towards an MREC submission at the end of October/beginning of November for a pilot and he came and it was halted. Now it may be no bad thing that it was delayed but it is damaging to the reputation of UK Biobank as it is one delay after another and we are losing good will with those liaising with the PCT's, service providers, areas where we were holding clinics, one RCC had even booked in time to run a pilot and it had to be cancelled which meant that Biobank lost face and did not come out of it too well [E2002; p. 10; p. 3].

Spoke members also attributed their lack of trust in the funding bodies and UK Biobank Limited to the nature of the changes, specifically their effect on the role of spokes in the initiative. They felt frustrated that their involvement was suddenly ended, having invested their efforts in the initiative for a number of years. For example, another spoke member reflected:

My services as an academic have been essentially no longer required ... my ability to input and obtain benefit from the research programme has been effectively stopped, and there is no resource despite having been a member of a successful bidding consortium for a sum of money which was originally envisaged at around 9 million pounds ... I think the way in which they have, seems to me, disregarded the university organisations who've engaged with the project until now is really very, very unhelpful [E2005; p. 17-18; p. 1-3].

Similarly, E2007 commented:

We were meant to be working on setting up the pilot, we put in quite a lot of work over the years thinking about how things would go ahead and it was all essentially guillotined and told we wouldn't really be involved in any of it...people felt very let down [E2007; p. 26; p. 4].

In criticising the implementation of the changes, some spoke members felt that the changes had a detrimental effect on the collaborations achieved between academic

scientists from different institutions in spoke formation. They argued that their negative experience of being a spoke for UK Biobank would make academic scientists less willing to collaborate in future scientific enterprises. For example, E2005 continued: ‘we had to make quite a lot of decisions on the basis of trust and for Biobank then to withdraw that basis really jeopardises the relationships that have been so precariously balanced and that I think is unhelpful’ [E2005; p. 17; p. 1].

## 6.6 Conclusion

The origins and development of UK Biobank were marked by a gradual erosion of trust between academic scientists and representatives of the funding bodies and UK Biobank Limited. The lack of trust manifested in protocol development and steadily diminished through the spoke bidding process to contract negotiation and organisational changes. Various reasons for the erosion of trust included criticism of the consultation process, criticism of academic scientists' motivations for involvement, lack of spoke payback via access to the resource, lack of clarity in the organisational structure, and the implementation of the organisational changes.

Academic scientists felt that the funding bodies and UK Biobank Limited did not trust them to develop UK Biobank as the funders and representatives of UK Biobank Limited allegedly did not undertake a genuine consultation process regarding protocol development, provide sufficient clarity surrounding the organisational structure or implement the organisational changes appropriately. Academic scientists' consequent lack of trust of the funding bodies and UK Biobank Limited was exacerbated by the latter's policy on spoke access. Academic scientists interpreted the implementation of the changes as the culmination of their experience of the origins and development of UK Biobank. They argued that the allegedly abrupt announcement and lack of consultation regarding the changes confirmed their suspicions of the funding bodies and UK Biobank Limited. Representatives of the funding bodies and UK Biobank Limited defended the consultation process and organisational structure. They accused academic scientists of being unnecessarily suspicious and overplaying their role. Any trust that the funding bodies and UK Biobank Limited placed with academic scientists to develop UK Biobank was shaken by their perceptions of academic scientists', particularly spoke members', motivations for involvement during the spoke bidding process, ongoing protocol development and contract negotiation.

An overarching explanation for mistrust between academic scientists and representatives of the funding bodies and UK Biobank Limited was different understandings of standard academic scientific practice. Academic scientists' criticism of the funding bodies and UK Biobank Limited largely concerned their alleged failure to understand standard academic scientific practice. They argued that

the funding bodies and UK Biobank Limited did not understand academic scientists' requirements to justify involvement in research activities to their employers in terms of the RAE. Similarly, the funding bodies and UK Biobank Limited did not seem to appreciate the alleged inappropriateness of academic scientists acting as service providers to UK Biobank Limited especially without financial or intellectual payback. This issue was complicated by academic scientists' different understandings of the appropriate role for academic scientists in research activities. Mistrust between academic scientists and representatives of the funding bodies and UK Biobank Limited could however be attributed to different understandings of UK Biobank rather than standard academic scientific practice. It could be argued that tension between the groups on the issue of spoke payback for example reflects the funding bodies' and UK Biobank Limited's failure to make clear to academic scientists how UK Biobank was different from other scientific enterprises.



## **Chapter 7**

### **Conclusion and Discussion**

#### **7.1 Introduction**

In this chapter I first summarise the thesis to remind the reader of the key points and aid understanding of the forthcoming discussion and conclusions. Second, I discuss my findings in the context of Big Science. I examine how UK Biobank could be regarded as a Big Science initiative and compare its origins and development to that of other Big Science projects. I also speculate as to the undocumented rationale behind selection of some of the most controversial aspects of the organisational structure. Third, I present my conclusions regarding the organisational issues that shaped the configuration of UK Biobank: leadership, the hub and spoke model and ambiguities within the organisational structure as a whole. Fourth, I reflect upon the strengths and limitations of my research, before finally considering potential future directions of this research.

## 7.2 Thesis Summary

UK Biobank, a resource set up in 2002, emerged amidst the promise associated with the completion of the HGP. Its aim was to gather genetic and lifestyle information from half a million participants aged 40-69 years old in the UK and monitor their health for up to thirty years in order to improve prevention, diagnosis and treatment of major diseases. The publication of a working draft of the human genome sequence in February 2001 challenged scientists to translate the abstract knowledge collected in the Project into practical benefits for human health. UK Biobank represented one such response to this 'post-genome challenge'. National genetic databases were a significant feature of international responses to the 'post-genome challenge'; projects were set up or proposed in Iceland, Estonia, Latvia, Sweden, Singapore, Tonga, Spain, and the United States. Like UK Biobank, these international endeavours were established to improve human health through improved drug treatments and personalised medicine. The Icelandic project was the most controversial because of its commercial nature and opt-out consent policy. This controversy fostered a concern amongst proponents of other national genetic databases to implement thorough ethical procedures to distinguish themselves from the Icelandic project. Ethical concerns, specifically over access to the sequence, also marked the development of the HGP. Hence, UK Biobank emerged in the context of two scientific enterprises, the HGP and the Icelandic database, that raised considerable ethical issues and consequently shaped its development.

In undertaking a contemporary history of the origins and development of UK Biobank, I charted its genesis from the first official meetings within the MRC in 1998, to the funding decision in 2002, through implementation of the organisational structure in 2003 and 2004, until the organisational changes in 2005. I have explored how and why UK Biobank was initially configured in the way it was, and focussed on the organisational aspects of its establishment. In the course of my study, the aim of my thesis changed in the light of interviewees' responses and the development of UK Biobank itself. I initially intended to analyse how, when and from whom the idea for UK Biobank emerged in the UK but interviewees largely ignored these issues and instead concentrated on the practical set up of UK Biobank. Also, the considerable time delays that accompanied UK Biobank (see table 2.8) meant that I could not

analyse its implementation, prompting my change of focus to UK Biobank's origins and development.

I enriched my understanding of the origins and development of UK Biobank by analysing the development of the history of contemporary science as an academic field. By exploring the contested nature of the history of contemporary science and scientists' expectations of its legitimising function in particular, I obtained a greater knowledge of the methodological issues associated with my study. Given UK Biobank's association with Big Science, analysis of the phenomenon proved useful. Reviewing characteristics and criticisms of Big Science and the origins and development of similar projects increased my understanding of the wider context surrounding UK Biobank and allowed me to determine the extent to which UK Biobank represented Big Science. Analysis of the organisational issues (such as leadership) characteristic of the development of Big Science projects proved especially relevant in my research.

The first official workshop between the MRC and the Wellcome Trust regarding what became UK Biobank took place on the 14 May 1999. It concluded that a new cohort should be established and recommended the establishment of the EWG to develop its outline. The EWG met between August 1999 and January 2000 and consisted of senior academic scientists. Their Final Report (published in March 2000) recommended the establishment of two new UK Population cohorts: an adult cohort to examine genetic and environmental risk factors and their interaction for common multi-factorial diseases of adulthood; and a birth cohort, but stressed the higher priority of the former. MRC Council and Wellcome Trust Governors approved the report in spring 2000 and agreed in principle to fund the proposal for UK Biobank whilst rejecting the birth cohort proposal in June 2000. The funding bodies set up the PDC in May 2001 to produce a draft protocol for UK Biobank for international peer review. The PDC met on five occasions between May and December 2001. The first draft of the protocol was produced on the 12 October 2001 and following discussion was sent for peer review in December 2001. Consultation exercises with a variety of groups including industry, interest groups, scientists, health workers, general practitioners, and the public were undertaken by the funding bodies directly, and by research groups and consultancies on their behalf between 2001 and 2003. The MRC

and the Wellcome Trust made the decision to fund UK Biobank in March 2002. The hub and spoke model that formed the basis of UK Biobank's organisational structure was established in March 2003. The main committees related to this model (the BoD, the Science Committee and the EGC) were set up between 2003 and 2004. The hub (also known as UK Biobank Limited) and its CEO were appointed at the same time as the spokes. This organisational structure changed in 2005 when significant alterations were made to the hub and spoke model.

UK Biobank's development was subject to considerable delays. For example, the appointment of the BoD, the Science Committee, the CEO, and the hub and spokes as well as the implementation of the pilot studies and recruitment were delayed. The proposal for UK Biobank was considerably developed after internal consideration within and between the funding bodies and consultation with the EWG, prior to the establishment of the PDC. The funding bodies' and EWG members' backing was secured before many of the academic scientists who would develop and implement UK Biobank were even aware of it. The funding bodies therefore sought to develop UK Biobank collaboratively only after having decided to fund it (albeit provisionally), which caused academic scientists to question the value of the consultation undertaken with them in protocol development. The simultaneous appointment of the hub and spokes caused a great deal of confusion as the relationship between the two unfolded. The spokes' role in UK Biobank was never formally agreed and contracts between the hub and the spokes were never signed, which contributed toward the lack of recruitment of participants under that model. Tension between spoke members and representatives of the hub and funding bodies was exacerbated by the organisational changes in 2005. I was surprised not to find any documentation nor interviewees' recollections regarding the origins of the hub and spoke model and this made it difficult to explore the rationale behind the selection of such an important feature of the initiative.

I conducted 76 oral history interviews; 64 were part of my main study and 12 were follow-up interviews. I approached and interviewed academic scientists directly and indirectly involved in UK Biobank, representatives of all four funding bodies and representatives of UK Biobank Limited (the hub). Interviews with academic scientists directly involved included spoke and committee members (from existing and former

committees). Academic scientists indirectly involved in UK Biobank included unsuccessful spoke bidders and members of the academic scientific community outside UK Biobank (critics and former spoke members). I conducted follow-up interviews with a sub-sample of the original participants in response to organisational changes in 2005, specifically spoke and committees members, and representatives of the funding bodies and UK Biobank. I adopted considerable confidentiality procedures to protect interviewees' identities, such as the use of descriptors, adoption of the generic 'he' pronoun throughout the thesis, and returning transcripts to respondents.

I conducted archival analysis of the MRC's official documents concerning the origins and development of UK Biobank. I applied to the Wellcome Trust for access to their official documents, but this was not granted. The MRC documents included official minutes of meetings of previous committees significant in the development of UK Biobank (such as the EWG and PDC), emails between committee members, representatives of the funding bodies and committee members, senior representatives of the funding bodies and MRC colleagues, and official correspondence (such as feedback to unsuccessful hub and spoke bidders). The coverage spanned from 1998 until 2004, reflecting the increasing role of the hub and the diminishing role of the MRC in taking UK Biobank forward.

I adopted a broad thematic approach to analysis of the interview material and archival research. Once I had coded the interview transcripts and took notes from archival research pertaining to key themes (such as the organisational model), I summarised every interview and the archival findings. I then grouped material from each of these themes into three broad areas that formed the topics of the three findings chapters: standard academic scientific practice, control and trust.

Academic scientists, who were previous and current committee members and spoke members, criticised the establishment of UK Biobank for departing from what I have called 'standard academic scientific practice'. Representatives of the funding bodies or UK Biobank Limited only referred to standard academic scientific practice when discussing the organisational changes. Academic scientists argued that UK Biobank represented such a departure for the following reasons: the funding decision was not

based on the production of a finalised protocol; the funding bodies took key protocol decisions prior to consultation with academic scientists, hence consultation was not genuine; the funding figure did not include the complete costs for UK Biobank; the funding bodies were too actively involved; the EGF was developed in tandem with the scientific protocol; there was no PI or product champion; the hub was established as a charitable company (UK Biobank Limited); the hub and spoke bidding process was confusing and secretive; temporary committees were established as predecessors to permanent committees; the hub, spokes and CEO were appointed prior to the BoD; and lastly, considerable organisational changes were made suddenly and following a number of years of effort to develop the original organisational structure. Academic scientists' criticism of the establishment of UK Biobank as departing from standard academic scientific practice is however complicated by different understandings of the term.

All constituent groups of interviewees described lack of clarity regarding who was in control of UK Biobank. Academic scientists and representatives of the funding bodies and UK Biobank Limited cited different explanations for the alleged confusion and held different opinions of where control lay. Academic scientists argued that the funding bodies held an unjust position of control and were too involved (citing the funding bodies' role in protocol development as evidence) and associated this with the ambiguity. Representatives of the funding bodies downplayed the extent of their role and argued that their own involvement diminished following the set up of the hub. Given their financial obligations, the funding bodies did however argue that some level of involvement was necessary. Academic scientists and representatives of the funding bodies and UK Biobank Limited attributed the confusion over control to a lack of leadership but in different ways; the former cited a lack of academic leadership in the form of a PI and the latter to a lack of managerial leadership. Academic scientists were used to control lying with a PI and felt that the adoption of a hub and spoke model contributed to the confusion over control as the role and responsibilities of the hub and spokes were not clear. Representatives of the funding bodies established the hub as a charitable company to ensure that it was free from any particular individual's or group's control. All constituent groups interpreted the organisational changes in 2005 as resolving the confusion over control but they viewed it differently. Academic scientists argued that as the funding bodies

orchestrated the changes, the changes reinforced their control whereas the funding bodies argued that UK Biobank's changing requirements meant that greater control over UK Biobank by an individual was necessary.

The origins and development of UK Biobank were marked by a lack of trust. Representatives of the funding bodies and UK Biobank Limited did not appear to trust academic scientists to develop UK Biobank, as they questioned the scientists' motivations for becoming involved. Academic scientists felt that the funding bodies and UK Biobank Limited did not trust them to develop the resource, citing the consultation process and organisational structure as evidence. In turn, they could not then trust the funding bodies and UK Biobank Limited. Academic scientists gave the following explanations for the erosion of trust between them and the funding bodies and UK Biobank Limited: lack of genuine consultation in protocol development; lack of understanding of spoke members' professional and financial obligations in becoming involved in research activities; lack of spoke payback; confusion over whether spokes would be granted payback; lack of clarity in the bidding process; confusion over the role of spokes; confusion over the nature of UK Biobank Limited; and implementation of the organisational changes. Representatives of the funding bodies and UK Biobank Limited defended the consultation process and organisational structure. They accused academic scientists of being overly suspicious and overplaying their role. The trust that the funding bodies and UK Biobank Limited had in academic scientists was shaken by their belief that spoke members' had 'non-scientific' motivations for involvement in UK Biobank, namely professional and financial obligations to host institutions.

The legacy left by the configuration of UK Biobank was one of considerable difficulty for academic scientists and representatives of both the funding bodies and UK Biobank Limited alike. Organisational issues, typical of those confronting Big Science initiatives, were largely responsible for this difficult legacy. Although the exact origins of the most controversial aspect of the organisational structure, the hub and spoke model, were not documented, I argue that it was borne out of the ethical concerns surrounding the HGP and the Icelandic database, namely a desire to be inclusive of a range of academic scientists. Leadership, the hub and spoke model and ambiguities within the organisational structure as a whole were the most significant

issues in the origins and development of UK Biobank as the organisational changes in 2005 testify.

Conducting a contemporary history of an evolving initiative presented opportunities and challenges that the historian of earlier periods or of more completely implemented initiatives would not face. For example, although undertaking a contemporary history meant that I overcame some of the problems associated with memory and viewed documents that might not be available to future historians, I had to protect interviewees' identities and analyse non-archived documents. As UK Biobank was an evolving initiative, I had the opportunity to probe further into the changing environment whilst managing the uncertainty associated with it. The positive response rate to interview requests and access to archival research were key strengths of my study design whilst the low number of follow-up interviews compared with the main study and archival research in only one funding body were limitations. Given the evolving nature of UK Biobank, there are many opportunities for extending this research.



### 7.3 Wider Context

The thesis summary above pointed to a number of key issues that permeated the set up of UK Biobank, such as leadership and lack of communication, which largely concerned the organisational structure. Academic scientists, the funding bodies and UK Biobank Limited invested a considerable amount of effort over a number of years to fully implement the hub and spoke model and recruit a half-million participants. Yet much of this effort was somewhat unproductive and all groups faced considerable difficulties and delays because fundamental issues were not resolved. For example, the relationship between the hub and the spokes, and the latter's role in UK Biobank, were not formally agreed prior to hub and spoke selection. Hence, once the hub and spokes were appointed a lot of time and energy was spent on attempting to resolve these issues rather than on recruitment. Ultimately, these issues were not resolved within the original organisational model, which prompted the organisational changes and underlines the extent of misdirected effort. Crucial decisions regarding the choice of organisational structure were taken at an early stage in the origins of UK Biobank: for example, selection of the hub and spoke model, observance of EU Procurement Rules in the hub and spoke bidding process, and timing of hub and spoke appointments. These decisions were responsible for many of the difficulties in the original organisational structure that contributed to the considerable time delays and sparked organisational change. In this way, UK Biobank's configuration left a difficult legacy for implementation of the resource.

Many of these organisational issues that shaped UK Biobank's origins and development are typical of those confronting Big Science initiatives. I will therefore discuss the origins and development of UK Biobank in the wider context of Big Science. First, I consider how UK Biobank could be regarded as a Big Science project before exploring how its origins and development compared with that of other Big Science projects. I will end this discussion with some speculations regarding broader explanations for the configuration of UK Biobank.

### 7.3.1 UK Biobank and 'Big Science'

#### *UK Biobank – a Big Science initiative?*

Each of the characteristics of Big Science explored in the literature review in 1.5.2 (scale, social and political context, sponsorship and organisational issues) can be applied to the origins and development of UK Biobank, which could therefore be regarded as a Big Science initiative. Scale was a significant issue and the half-million sample was important scientifically and politically. Much of the enthusiasm surrounding the origins of UK Biobank focused on it being the 'world's largest' genetic database. The social and political context surrounding UK Biobank was also characteristic of Big Science. The funding bodies stressed the political approval for UK Biobank, and supportive comments from politicians accompanied the 2002 press release announcing the commitment of funds. UK Biobank raised a number of ethical issues regarding the use of genetic information, and this ethical dimension underlined the social context of UK Biobank. Furthermore, the significant costs involved in the initial phases of UK Biobank, approximately £62 million, justifies its description as a Big Science project. Scientists' fears that funding UK Biobank would be detrimental to the funding of other smaller scale projects because of the costs involved is also typical of concerns surrounding Big Science. Moreover, government sponsorship of UK Biobank, indirectly via the MRC and directly through the Department of Health, is also characteristic of Big Science. Finally, organisational issues that characterise Big Science projects were also evident in the set up of UK Biobank. Tension over issues such as centralisation, leadership, control and organisational styles marked the origins and development of UK Biobank.

There were some aspects of UK Biobank that were not indicative of Big Science: for example, given the social and political context, the role of product champion is crucially important in Big Science initiatives yet there was no such figure who advocated for UK Biobank throughout its origins and development. Industrial sponsorship is a further area where UK Biobank could be said to depart from Big Science initiatives. Although industrial groups were consulted, they were not involved in developing the resource via protocol development nor did they sponsor UK Biobank. Nonetheless, there is enough common ground to describe UK Biobank as Big Science.

*How does the origins and development of UK Biobank compare with that of other Big Science projects?*

Before I address this question, I should point out the difficulty involved in comparing Big Science projects. As Big Science projects tend to differ quite considerably in nature and context, drawing comparisons between them is difficult. Given the resources involved, the origins and development of Big Science projects are considerably shaped by the social and political environment at the time. Pestre and Krige, for example, have stressed the difficulty of presenting the development of CERN as a model to be emulated due to its individuality and position as the first postwar European collaborative scientific endeavour: ‘the specificity of the case, the circumstances surrounding its birth, and the unique nature of its research facility in Europe indicate that the species could not - and would not – be reproduced easily’ (Pestre and Krige 1992) (p. 87). Furthermore the considerable scientific differences between Big Science projects can limit the extent to which valid comparisons can be made. David Edge and Michael Mulkay point to the difficulties of assessing the influence of scientific differences in making direct comparisons:

direct comparisons between our study [on the emergence of radio astronomy in Britain] and sociological studies of other scientific specialities that do not share similar technical characteristics are likely to be unproductive, unless the effects of such technical differences can be adequately assessed and discounted (Edge and Mulkay 1976) (p. 346).

Bearing this in mind the following comparison of the origins and development of UK Biobank with the Big Science projects described in 1.5 (MRC AIDS Directed Programme, CERN, The Space Telescope and the HGP) can only be made at quite a general level.

UK Biobank lacked a product champion who advocated for the resource throughout its birth and development. There was no single figure identifiable with UK Biobank who drove the resource forward or undertook a leading role in its development. It was initially driven by the leaders of the two main funding bodies, the MRC and the Wellcome Trust, who were approaching retirement at the time. This is in contrast to other Big Science projects. For example, Sir James Gowans was instrumental in gaining funding and support for the MRC AIDS Directed Programme and was its first

Director. Raoul Dautry and Pierre Auger played significant roles in the establishment of CERN and continued to be influential as Council members in their position as the ‘founding fathers’ of the project. Indeed the leading role taken by scientists in CERN’s origins and development through the Council have been associated with its success. Lyman Spitzer united ground and space based astronomers around the idea of the Space Telescope and garnered political support for the project that secured its establishment. The HGP was championed by high profile figures, such as James Watson and John Sulston, who not only played important roles in getting the initiative underway by securing funding, but also guided it through a difficult development that included a threat from industry.

UK Biobank has many potential endpoints and no clear marker of success. For example, the beginning or ending of recruitment or the beginning or ending of follow-up could all be regarded as a successful outcome of the endeavour. Partly because it represented ‘resource science’, its overall purpose, other than to set up a database, was relatively ambiguous. Even the establishment of another resource, a nuclear physics laboratory, in the case of CERN was set up with a clear initial aim to build a particle accelerator. The Space Telescope Project aimed to build and launch a telescope into orbit and although, like UK Biobank, it did not represent research in itself, this clear aim lent it focus. The mapping and sequencing of the human genome was the clear outcome and ‘big’ question of the HGP. An overarching aim of the MRC AIDS Directed Programme was to find an AIDS vaccine and although this was not realised it focussed the project. These projects therefore had clearer markers of success than UK Biobank.

Although UK Biobank was a response to the ‘post-genome challenge’ to justify the abstract knowledge gained in the HGP it lacked a sense of urgency, which is reflected in the time delays that marked it. Early on in its origins funds were committed in principle and the funding decision itself did not follow the production of a final protocol. Therefore much of its development came after funds were committed, which perhaps contributed to a lack of urgency. The emergence of the AIDS Directed Programme amidst the 1986-87 policy period of ‘national war-time emergency’ coupled with the possibility of finding a vaccine lent the Programme considerable potency (Berridge 1994) (p. 135). The struggle to gain Congressional funding for the

Space Telescope united astronomers into securing funding. Competition with the US accompanied the origins of CERN and their initial aim of constructing the biggest accelerator in the world. This element of a ‘race’ also drove the HGP as scientists in the publicly funded international effort competed with those of private industry (Celera) to map and sequence the human genome.

Collaboration between spoke members in recruitment and ongoing protocol development was an important part of UK Biobank’s original organisational structure. The funding bodies brought academic scientists from all over the UK who represented a range of professional backgrounds (including general practice, epidemiology and psychiatry) and opinions together to set up UK Biobank. This collaboration resonates with the development of the Space Telescope whereby product champions brought sceptical ground-based astronomers together with space astronomers and united them in the common goal of securing funds. International collaboration was a feature of both CERN and the HGP.

UK Biobank was not a hypothesis driven research endeavour, which in itself is not particularly uncommon in Big Science. For example, the Space Telescope and the HGP were not developed with specific hypotheses in mind. However the effect of a lack of hypotheses combined with confusion in the original organisational model caused considerable difficulties in the development of UK Biobank. As academic scientists were unsure of the purpose of UK Biobank and their role within it, they endeavoured to impose hypotheses that would address what they saw as research priorities. The funders saw these efforts as attempts to take control of UK Biobank, which contributed toward the breakdown of trust between the funding bodies and academic scientists. Although the HGP was criticised for its lack of hypothesis, there was a ‘big question’ that guided it, which, it could be argued, helped to prevent such major complications. In the development of the Space Telescope, astronomers utilised its lack of hypotheses to widen participation in the initiative and thereby increase political support. The involvement of astronomers, rather than funding bodies, in determining its nature and uniting to secure funds for the project could explain why its lack of hypothesis was not damaging.

Academic scientists argued that the funding bodies had already decided on key aspects of UK Biobank's design before consulting them. For example, they argued that the half-million sample size was a political decision that was heavily publicised early on and therefore non-negotiable. It could then be argued that the parameters of UK Biobank were firmly set at an early stage in its development. This resonates with the origins of the Space Telescope, whereby astronomers made a number of significant changes to the project to secure political and financial support. For example, the reduction in the size of the primary mirror determined and had considerable ramifications on its future development and meant that the Space Telescope was 'trapped by its own history' (Smith 1989) (p. 186). Consideration of this issue begs a crucial but as yet unanswerable question: can UK Biobank escape its history, and can a useful resource that will benefit human health be successfully established?

### 7.3.2 Broad speculative explanations for the configuration of UK Biobank

Given the significance of the hub and spoke model in the origins and development of UK Biobank and the lack of documentation regarding its selection (see 7.4), it is necessary to make informed speculation as to why it was chosen. Based on comments from all groups of interviewees, I believe that senior representatives of the funding bodies selected a hub and spoke model primarily to involve a wide range of academic scientists in the resource as well as to foster regional recruitment. In selecting this model, the funding bodies ensured that academic scientists throughout the UK from various professional backgrounds were represented, and thereby avoided any potential criticism that would arise if academic participation was restricted to a single group. I argue that this concern for fairness was partly borne out of the ethical concerns that surrounded the issue of access to the human genome sequence and the controversy that accompanied the Icelandic database.

It could be argued that many of the difficulties surrounding the hub and spoke model were caused by the way in which it was implemented rather than any intrinsic flaws in the model itself. For example, much of the tension between the funding bodies and academic scientists in the hub and spoke bidding process could have been avoided if EU Procurement Rules had not been observed. These rules made the bidding process

far more complicated and the secrecy that they demanded aroused considerable controversy. Like the hub and spoke model, there was confusion regarding why the rules were observed. Some funding body representatives claimed that they were legally obliged to follow them whilst others claimed that this was not the case. Perhaps a determination to make the bidding process fair and transparent motivated the funding bodies to observe EU Procurement Rules. Ironically, these rules resulted in a confusing bidding process that fostered a sense of suspicion on the part of academic scientists who were unfamiliar with them.

UK Biobank's emergence amidst the ethical concerns wrought by the HGP and the Icelandic database therefore had considerable consequences for its configuration. This context not only accounted for the extensive consultation exercises with the public and professional groups and early development of the EGF in tandem with the scientific protocol, but it may also have resulted in key organisational decisions, such as the selection of the hub and spoke model or following EU Procurement Rules.

Given the costs and political context of Big Science, particularly in the case of government sponsorship then perhaps such organisational difficulties and tensions between academic scientists and funding bodies are intrinsic to Big Science. Certainly, the comparison above points to a number of common issues such as collaboration and the importance of leadership (illustrated in the case of UK Biobank in the problems caused by a lack of leadership). Furthermore issues of trust between funding bodies and academic scientists are indicative of all science, big and small. However, the way in which these difficulties manifest varies considerably between Big Science projects, which coupled with the problems involved in making direct comparisons between Big Science initiatives renders analysis of the particular configuration of UK Biobank in its own terms very important.

## 7.4 Conclusions

These conclusions concern the organisational issues that influenced the set up of UK Biobank. I conclude that leadership, the hub and spoke model and ambiguities within the organisational structure as a whole were the most significant issues in the origins and development of UK Biobank. Such was their importance that each of these issues was addressed in the organisational changes of 2005; Rory Collins was appointed as PI and CEO, the hub and spoke model was substantially altered and much of the confusion that surrounded the organisational structure was removed as a result. Given that the ultimate success or failure of UK Biobank's establishment cannot be assessed for many years, and the difficulty involved in selecting adequate criteria with which to judge its set up, these conclusions are however preliminary.

### *Leadership*

The lack of product champion or leader was one of the most significant aspects of the original organisational structure that impacted on the development of UK Biobank. The resource suffered from a lack of identity as there was no single figure active within the academic scientific, political or industrial community who advocated for UK Biobank. The then leaders of the MRC and the Wellcome Trust, Sir George Radda and Dr Mike Dexter, who initially drove the idea for UK Biobank, were near retirement at the time and retired very soon after the funding decision in 2002. Some senior academic scientists heavily involved in the origins of UK Biobank, such as Tom Meade who chaired the EWG, were also near retirement during their involvement. This lack of identity contributed to UK Biobank's low profile and lack of urgency. Unlike the development of the Space Telescope there was no figure equivalent to Lyman Spitzer to unite academic scientists, and particularly critics, around the idea.

Decision making, particularly in ongoing protocol development following the funding decision, was diffused. Large groups of academic scientists were involved in the Science Committee and its various sub-groups, and the difficulty of reaching consensus was a major factor in the delays that affected set up of UK Biobank. The lack of a leader responsible for making decisions had a substantial influence. A further implication of such lack of leadership was confusion over who was in control



of UK Biobank, and consequent tension between academic scientists and the funding bodies. Several academic scientists pointed to alleged difficulties that the former CEO, John Newton, faced in asserting his authority over UK Biobank because of the funding bodies' control over his appointment and the resource generally. For example, some stated that even once he was appointed, albeit unofficially, the funding bodies did not inform him of the location of the hub that he would manage. Hub bidders were not required to nominate a CEO from their host institution, rather the funding bodies choose a CEO from Oxford rather than Manchester (the location of the hub), which further hampered his control of the resource. There was therefore no central authority figure easily recognisable as taking control of UK Biobank such as there was in the case of CERN with its powerful Council and Director General.

#### *Hub and spoke model*

The hub and spoke model was responsible for most of the difficulties in the original organisational structure as its removal following the organisational changes in August 2005 testifies. It is perhaps telling of the ambiguity that surrounded the organisational structure that the rationale for the selection of this controversial model was not documented. There was no record of any debate surrounding the choice of model in the documents I analysed. It is therefore difficult to say how it came to be adopted. It was however an integral part of the origins of UK Biobank and was referred to in the EWG Report of March 2000 and the Draft Protocol of October 2001. With regard to the origins of the hub and spoke model, all constituent groups of interviewees pointed to the national nature of UK Biobank in terms of the model facilitating regional recruitment and inclusion of a wide range of academic scientists (see 7.3 for informed speculation regarding its selection). They could not however articulate where exactly the idea for it came from in terms of there being any precedents for it or how it came to be adopted.

Lack of spoke 'payback' for spoke members' role in recruitment and ongoing protocol development was the overriding problem with the model. Confusion over whether or not spokes would get payback and criticism of the policy itself set a tense tone that accompanied the development of UK Biobank. Spoke payback was an unresolved issue and an unremitting source of tension between academic scientists on the one hand and the funding bodies and UK Biobank Limited on the other. Academic

scientists were particularly frustrated at the apparent misunderstanding that the policy showed of their professional and financial obligations to host institutions. They stressed the significance of these obligations in terms of how their merit as academic scientists is measured in terms of performance indicators such as publications and grant income. Tension over the issue manifested in academic scientists' criticism of UK Biobank as departing from standard academic scientific practice and in the lack of trust between them and the funding bodies in particular.

The manner by which the hub and spoke model was set up was another source of difficulty, which had far-reaching consequences. The hub, spokes and CEO were appointed simultaneously in March 2003. Given that the CEO would manage the hub, and the hub would direct the spokes, simultaneous establishment meant that the CEO and the hub could not function in their intended role. Initially, the CEO and the hub did not have an infrastructure or sufficient resources with which to direct the spokes and were unable to do so for some time after their appointment. The CEO experienced further difficulties in establishing his authority as he was not involved in selecting the hub that he would direct, which exacerbated the problems involved in simultaneous appointment. Considerable time delays as the CEO and hub became established and difficulties in the relationship between the hub and the spokes as the former struggled to assert authority were the key implications of the manner by which the model was set up.

The hub and spoke bidding process left a damaging legacy and contributed toward the breakdown of trust between academic scientists and the funding bodies. The funding bodies' decision to adopt EU Procurement Rules for the bidding process was the key difficulty as it rendered the process secretive. Academic scientists were not used to this type of secretive environment and were generally not familiar with EU Procurement Rules. This meant that they did not understand why the process was so complicated and assumed that the funding bodies were directly responsible for the secrecy. This confusion illustrates the difficulties caused by a lack of communication between the funding bodies and academic scientists over EU Procurement Rules. Adoption of EU Procurement Rules compromised the collaborative process that the funding bodies encouraged between spokes after selection as it followed a complicated, highly competitive and secretive tendering process in which discussion

between different hub and spoke applicants was expressly forbidden. Like the origins of the hub and spoke model, it is not clear exactly why the funding bodies followed EU Procurement Rules. The archival documents I accessed did not contain details of any debate surrounding their adoption. The funding bodies argued that they were legally obliged to undergo EU Procurement Rules, but some senior academic scientists who were aware of the Rules disagreed and stated that they did not know why the funding bodies adopted them. In other large scale areas of funding the MRC and the Wellcome Trust have not used EU Procurement Rules (for example UK Clinical Research Collaboration's (UKCRC's) call for centres of excellence in public health research in 2007 and the ESRC and MRC have annual competitions for centres without adopting this EU process).

#### *Ambiguity in the organisational structure*

Ambiguity within the organisational structure and the hub and spoke model in particular complicated the development of UK Biobank. As academic scientists did not know who was responsible for decision making within the resource (particularly with regard to protocol development and the hub and spoke model) they felt powerless to influence its development. The lack of clarity regarding the role of spokes and whether this role extended beyond recruitment to undertaking regional sub-studies frustrated spoke members who found that their interpretation of their role did not correspond with that of the funding bodies and UK Biobank Limited, which contributed toward the reduction in trust between them. The implications of these confusions were difficult to overcome, and in the case of the hub and spoke model proved insurmountable, which contributed to the considerable time delays in the set up of UK Biobank.

Ambiguities regarding the hub and spoke model were symptomatic of poor communication between the funding bodies and academic scientists. They reflected confusion on the part of academic scientists regarding the nature of UK Biobank itself, and the funding bodies' inability to articulate to academic scientists how it differed from a standard hypothesis driven research project.

Indeed, this analysis can be broadened out to the origins and development of UK Biobank in general. Poor communication, confusion and an organisational model that

was not sufficiently transparent led to the gradual erosion of trust between academic scientists and representatives of the funders. These problems instigated major change in the organisational structure at the highest levels, and removal of much of what was seen as controversial in the original hub and spoke model. Whether these changes will have the desired affect will become apparent as UK Biobank gets underway in earnest over the coming years.

## 7.5 Strengths and Limitations

The strengths and limitations of my research both mainly related to its contemporary historical nature and UK Biobank's status as an evolving initiative. There were also a number of advantages and disadvantages to the way in which I designed my study. In retrospect I believe the strengths of my research overcame the limitations and that the study design selected was the most appropriate option.

### 7.5.1 Contemporary history

In conducting a contemporary history of the origins and development of UK Biobank I encountered opportunities and challenges that the historian of earlier periods would not face.

Conducting a contemporary history allowed me to overcome some of the problems associated with memory. I interviewed respondents on their experience and opinion of events that took place within five to six years of the interview, along with events taking place at the time of the interview. The origins and development of UK Biobank were still fresh in interviewees' minds, especially those aspects of the development of UK Biobank unfolding at the time of the interview, such as contract negotiation between the hub and the spokes and ongoing protocol development. Conducting a contemporary history therefore gave me the opportunity to seek an understanding of the origins and development of UK Biobank that would not be available at a later stage. Future opinions and recollections might alter depending on the ultimate success or failure of UK Biobank, so I was able to capitalise on understandings that might not be available to later historians. I conducted oral history interviews with respondents when they did not know if UK Biobank would be a success or failure. This relates to the issue of 'composure' as discussed in chapter three. It was therefore difficult for interviewees to construct an account of the origins and development that corresponded with their present identities given the evolving nature of UK Biobank. I also conducted oral history interviews with senior players approaching retirement or already retired who may not be accessible to future oral historians.

The immediacy of UK Biobank meant that interviewees held and expressed strong opinions. The majority of interviewees were actively involved in the initiative at the time of the interview, carrying out some of the tasks that they commented upon and intimately involved in UK Biobank. This resulted in passionate responses to questions and some interviewees sought to clarify issues more fully. The advantage of conducting oral history interviews on events recently or currently experienced by respondents was reflected in the difficulty of engaging respondents who were no longer involved in UK Biobank. Oral history interviews conducted with those indirectly involved were generally less informative than those conducted with respondents directly involved. Interviewees who had not been actively involved for three to four years struggled to respond to questions, and could not muster much enthusiasm for the interview. Surprisingly, this also applied to unsuccessful spoke bidders who found it difficult to reflect on their experiences as their professional interests had developed, and they had no further contact with the initiative. As they were removed from the resource and had been for a number of years, their personal accounts were tightly constructed and corresponded strongly with their present identities. Those indirectly involved were also the most contented as they had moved on personally and professionally whereas accounts of those directly involved were dominated by their current experiences and UK Biobank's lack of progress.

Conducting a contemporary history gave me the opportunity to view documents to which future historians might not have access. As a contemporary historian, I had to negotiate access to documents that were not publicly available because of their 'live' status, and therefore not yet archived. As discussed in chapter three, this material contained duplicate and misfiled documents that often contained illuminating comments pencilled in the margins. It is unlikely that such documents would be preserved once the material is archived and therefore will not be available to future historians. The contemporary historian can therefore access information that once archived may not be available to future researchers. Smith reflected upon these advantages and disadvantages of analysing 'live' documents:

I have spent a considerable amount of time acting as my own archivist. However, the complications have their pluses as well as their minuses, because of the chance to study materials that might be destroyed shortly or thrown in the trash can (Smith 1989) (p. 419)

The challenges involved in conducting a contemporary history were often closely related to the opportunities it presented. Interviewees' enthusiasm on account of the contemporary nature of my research represented a challenge as well as an opportunity and managing strong emotions was difficult. Some interviews were difficult to control because of respondents' enthusiasm and eagerness to share their experience. Their zeal would manifest in attempts to drive the agenda of the interview, which could be problematic. Interviewees' attitudes toward UK Biobank often coloured their perceptions of the interview itself, and their frustration regarding UK Biobank manifested itself in aggravation toward my study. Although I was reassured by interviewees' explanations for such frustration, and understood them better as I conducted more interviews, these sentiments remained challenging.

It was also challenging to undertake research on the origins and development of an initiative that was not accompanied by a body of literature, which is attributable to the contemporary nature of my study. Lack of literature defined the nature of my research, and my study was exploratory on account of the lack of hypothesis. The potential for hypothesis testing in researching Big Science is further limited by the variation between different types of Big Science projects. Other accounts of Big Science projects are also exploratory; Edge and Mulkay commented in their history of the emergence of radio astronomy in Britain that 'we decided that we would not define in advance the detailed questions to be answered nor the precise research procedures to be adopted' (Edge and Mulkay 1976) (p. 5). They described the available hypotheses as 'few' and 'questionable' and pointed to the lack of relevant literature on the topic (Edge and Mulkay 1976) (p. 5).

Conducting a contemporary history of the origins and development of UK Biobank involved considerable responsibility to respondents and, given the controversy surrounding the resource, the ramifications of participation in my study could be significant. In light of such responsibility, I had to adopt procedures to protect interviewees' identities. These procedures are discussed fully in chapter three but suffice to say they proved challenging to implement as the vast majority of interviewees were actively involved in UK Biobank at the time of the interview.

Analysing non-archived documents was a further challenge and made archival analysis time-consuming on account of duplicate and misfiled documents. These issues are also addressed fully in chapter three but I will reiterate one of the difficulties involved here. Although documents were categorised in files with distinct reference numbers, such as ‘D550/10, Hub and Spoke Relationship, Biobank, Volume 1’, some of the categories were similar and referred to the same episodes, which resulted in misfiled documents.

### 7.5.2 Researching an evolving initiative

I encountered opportunities and challenges in my study on account of the evolving nature of UK Biobank, which underwent significant changes throughout my research. Significant modifications took place even prior to the organisational changes in August 2005. For example, the CEO of UK Biobank Limited, John Newton, resigned, groups were established and then disbanded particularly in ongoing protocol development, and new positions were created such as Spoke Coordinator. UK Biobank's evolving nature was underlined by the organisational changes in 2005. As discussed in the preface, the title of my PhD was originally ‘Lay and professionals’ experiences and views of the MRC/Wellcome Biobank Project’ but once I took up the studentship it changed to ‘A contemporary history of the origins and development of UK Biobank’ for the following reasons. It was envisaged that UK Biobank would have begun recruitment prior to commencement of my studentship, which would have allowed interviews to take place with participants. However, UK Biobank had not developed to that extent when my research began in October 2003. It was therefore agreed that I should not interview members of the public, not only because they had not begun to be recruited, but also on account of UK Biobank’s lack of public profile. These changes reinforce the flexibility required to undertake research on an evolving initiative.

Organisational changes were accompanied by significant alterations to the UK Biobank website in 2006. For example, archived press releases, the chronology, information regarding protocol development, and certain documents such as the draft protocol were removed. If UK Biobank had not been evolving, I would not have had the opportunity to access these documents and witness such changes. Furthermore,



future historians would be unaware of these alterations to the presentation of the resource, which indicates the opportunities involved in researching an evolving initiative and undertaking a contemporary history.

Conducting oral history interviews on an evolving initiative in some ways fostered a richer understanding of the origins and development of UK Biobank. As interviewees did not expect me to be familiar with the changing environment they felt compelled to explain it fully, which made interviews more informative. The changing environment thus rendered my study more important to interviewees who were keen to articulate the changes clearly for their benefit as well as mine. For example, following a long explanation regarding the development of the organisational structure, one interviewee remarked how it was the first time that he was able to articulate his thoughts clearly on a changing issue, and stated that he found it very useful. He commented: ‘Well, that’s the first time I’ve actually talked myself through that and I think that was pretty persuasive, I think I’ve persuaded myself’ [070; p. 1; p. 7]. Interviewees felt that the changing environment justified my research and their enthusiasm to explain the changes overcame hostility over the contemporary nature of my research and allowed me to probe deeper into the nature of the changes without incurring frustration. The changing environment thus gave me the opportunity to obtain a fuller understanding of the origins and development of UK Biobank than if the environment was static.

Historians of contemporary science face particular challenges in researching evolving scientific initiatives. These challenges offset some of the opportunities discussed. I found it difficult to keep up with the changing environment and remain informed regarding evolving circumstances, such as the formation of new groups of scientists. The difficulty of maintaining up to date knowledge on the development of the resource was exacerbated by some respondents’ uncertainties regarding the changing environment and interviewees’ accounts would conflict. Often, interviewees informed me of forthcoming changes before they were public, which meant that I had to react appropriately and handle the information suitably. For example, I had to maintain my composure and stay focussed on the interview schedule during an interview in which a respondent reported how John Newton (the former CEO) had just resigned, days before this information was released.

Uncertainty regarding the development of UK Biobank affected both archival research and oral history interviews. It meant that I could not focus my research too early and I had to assume that every document was potentially significant to my research. I also had to remain flexible regarding my interview schedule and update it according to changing circumstances. Interviewees' confusion regarding the changing environment represented a further challenge as it dominated some interviews. Some interviewees focussed on clearly articulating recent changes and speculating about future developments rather than concentrating on the questions in hand. It was difficult to change the focus of the interview from unfolding developments to past events. Often questions were interpreted in terms of the current situation at the time of the interview, rather than in terms of their background. For example, questions regarding the origins of the hub and spoke model were interpreted in terms of its current manifestations. Confusion regarding the changing environment was responsible for interviewees' frustrations toward UK Biobank, which manifested in hostility toward my study.

Uncertainty surrounding the development of UK Biobank was problematic as it subverted the roles of interviewer and interviewee. Some interviewees questioned my knowledge of the changing environment and implied that I was more aware than they were of developments. This reflected confusion regarding the nature of my research, and a perception that I was acting on behalf of the MRC. It also demonstrated the extent of the confusion and the desire of some interviewees to find out exactly what was going on. Such confusion was particularly challenging following the organisational changes and it was difficult to overcome these questions and focus on the interview itself. The evolving nature of UK Biobank also allowed interviewees to evade questions, and some, particularly senior, interviewees would avoid giving full answers on account of the changing environment. They argued that it was difficult to answer certain questions as UK Biobank was still developing. My interview schedule was however sensitive to the evolving nature of UK Biobank, and such reaction was indicative of misunderstanding regarding the role of my research as evaluating the scientific merit of UK Biobank. Reluctance to answer certain questions because of the evolving nature of UK Biobank was also attributable to unwillingness to comment on past events that remained unresolved. For example, some interviewees were not

prepared to discuss their experience and opinion of protocol development as the protocol was not finalised during the period of my research.

The evolving nature of UK Biobank renders any conclusions regarding its origins and development preliminary and I had to be aware of the impact of unfolding events on my research. As the future success or failure of UK Biobank is unknown and it will be many years before such an analysis could be made, I had to be careful. Smith encountered such difficulties in researching the development of the Space Telescope, and stressed the incompleteness of his account because of its evolving nature. Given that the Space Telescope was still in the observation phase when his book was published in 1989 he commented:

Certainly at this stage in the telescope's development, one cannot claim to have written a definitive account. Not only has the telescope's observing life to end, but its technology links to military spacecraft mean that a full analysis of its design heritage must await the lapse of many years (Smith 1989) (p. 4).

### 7.5.3 Study Design

The positive response to my requests for oral history interviews was a significant strength of my study. For example, in the main study 69 of the 89 approached agreed to an interview and 64 interviews took place, and all 12 of those approached for a follow-up interview agreed (totalling 76 interviews). It meant that my sample was composed of several representatives from each of the committees and groups involved in the origins and development of UK Biobank (see table 3.1). There were several advantages of this response and representation. I accessed a wide range of experience and opinion, which increased my understanding of the issues involved. I gained access to a range of individuals with varying degrees of involvement and different experiences of the initiative. For example, I interviewed people who had only been involved in the initiative for one or two years, as well as individuals who had been involved since the origins of UK Biobank in the late nineties. The large number of interviews (76 in total) itself encouraged participation in my study. The controversy surrounding the origins and development of UK Biobank meant that some respondents were unsure whether or not they should participate and many potential interviewees asked how many interviews I had carried out. I was able to reassure

these people by detailing the number of interviews carried out, and the type of people that I was contacting. The ability to protect individuals' identities was a key factor in a positive response rate. In carrying out a substantial number of interviews, and conducting interviews with several representatives of each committee and group, I could safely use material from most interviews without identifying any respondent.

Access to archival research was a further strength, which served as an advantage in its own right and complemented oral history interviews. In analysing archival documents, I gained insight into different understandings of UK Biobank's origins and development that were not available elsewhere. For example, some of the documents contained material that presented the opinions of senior individuals within UK Biobank who did not agree to an interview. These included letters to representatives of the funding bodies and personal contributions to meetings contained in the minutes. Although these documents did not allow as rich an understanding of experiences and opinions as may have been achieved in an oral history interview, they were helpful. As these documents were preserved by representatives of the MRC, analysis of them allowed insight into the inner workings of one of the main funding bodies of UK Biobank. This served to supplement understandings gained from oral history interviews with representatives of the MRC. Archival research complemented data from oral history interviews in a wider sense and it partly informed my topic guide. This was advantageous as it increased my knowledge of the issues involved in the configuration of UK Biobank, which made me a more informed interviewer. This increased understanding gained through archival research thus allowed me to probe more effectively. A further strength of archival research was the ability to compile an accurate chronology of the origins and development of UK Biobank. Access to clearly dated and presented documents meant that my chronology was not subject to the problems associated with memory.

The procedures adopted to protect interviewees' identities were advantageous. As discussed in chapter three, the most significant of these steps was the policy of not naming any interviewee and instead referring to respondents' general position in relation to UK Biobank such as 'member of the PDC'. Although this level of anonymisation is standard in sociological studies, it is unusual in historical projects. Giving respondents the opportunity to see a copy of the transcript and passages from

the thesis that quote extensively from their transcript was an asset. Interviewees were not only comforted by these procedures themselves, but were reassured by the consideration shown for their circumstances. These steps therefore encouraged participation and fostered a more open interview by allowing interviewees to speak frankly, which is reflected in the comments of a senior respondent. He explained if identifying him was more important than the content of the interview then he would agree to being identified, but would not be in a position to give an honest, full and frank account of his experience and opinion. I explained how the content of the interview was more important than being able to attribute the comments and a discussion of my procedures followed. This interview was one of the most important undertaken and demonstrated the advantages of the procedures adopted. If such steps had not been taken, the participation rate would have been lower and accounts less honest.

The decision to produce a conduct agreement regarding archival research at MRC Headquarters was beneficial. I agreed not to photocopy any documents, to return any files needed by staff, and to maintain the same hours as the individual responsible for the documents and my access to them. This agreement reassured staff at the MRC that I would handle the documents responsibly, which meant that I was not viewed as a threat. Such reassurance ensured that access to the documents was maintained and made the difficult process of arranging desk space in a busy corporate affairs office easier. The conduct agreement thereby facilitated access to the documents and was an important aspect of my study design.

Despite the positive response to my study, my understanding of the origins and development of UK Biobank could have been enriched by further interviews. The lack of response and refusal of some interviewees to my request for an interview was thus a limitation of my study design. For example, two of those who did not consent were key figures in the origins of UK Biobank whom other interviewees had recommended I interview. Two further individuals who did not agree to an interview played a significant role in the development of UK Biobank, specifically in organisational issues.

My sample was heavily weighted toward those directly involved in UK Biobank (59 of the 64 in the main study) and this imbalance was limiting. I conducted far fewer interviews with those indirectly involved in UK Biobank (unsuccessful spoke bidders, scientists not involved in UK Biobank). Interviewing equal numbers of those directly and indirectly involved might have resulted in a more balanced and informed study and would have addressed potential accusations of bias. This was not however possible due to the time constraints discussed and would have involved conducting a far greater number of interviews (approximately 120). It was imperative that I conducted such a large number of interviews with those directly involved to protect respondents' identities, and it would therefore have been very difficult to conduct fewer interviews with those directly involved to allow equal number of interviews with those indirectly and not involved to take place. The quality of interviews conducted with those indirectly involved further justified the decision not to approach equal numbers of individuals from both groups. I found that awareness, not to mention knowledge, of the initiative was heavily restricted to those directly involved.

I conducted a low number of follow-up interviews compared with the main study, 12 compared to 64, which limited my study. I could have gained a richer and more varied understanding of the nature of the organisational changes by conducting follow-up interviews with every respondent who took part in the main study. In doing so, I would have overcome some of the bias associated with selection of interviewees from the main study to approach for the follow-up interviews. Again however, the time pressures involved in PhD study would have made this very difficult. Furthermore, conducting follow-up interviews was not part of my original study design but was in response to considerable and unanticipated organisational changes that took place in the latter stages of my fieldwork. Although I only conducted 12 follow-up interviews there was a high degree of consensus amongst respondents, which suggests that interviewing every respondent from the main study again would not have been particularly informative.

Although the procedures adopted to protect interviewees' identities were advantageous and, I would argue, necessary in securing participation and open interviews, they were also limiting. Identifying respondents would have perhaps increased the potency and significance of my analysis, especially when attributing

comments to senior figures within the funding bodies or witnesses to the more controversial aspects of the origins and development of UK Biobank, such as protocol development. Protecting interviewees' identities was certainly a difficult task and led to the exclusion of some material from the thesis. In retrospect I believe that the advantages of the confidentiality procedures far outweighed the disadvantages. I argue that far from rendering my account more significant, identifying respondents would have resulted in a less powerful thesis as interviewees would have been prevented from giving an honest and full account of their experiences and opinions. Furthermore, I found that referring to interviewees by their involvement in UK Biobank was adequate.

Archival research was restricted to only one of the funding bodies and I was only able to access those documents relating to the origins and development of UK Biobank at the MRC. I was denied access to the Wellcome Trust's documents and did not pursue access to those of the DoH and the Scottish Executive. The archival research conducted was therefore biased toward the perspective of just one of the funding bodies. Access to the documents of the other funding bodies would not only have entailed analysing material not contained at the MRC, such as the minutes of meetings held at the other funding bodies' headquarters, but it would have given me the opportunity to view the configuration of UK Biobank from other perspectives. Archival research based solely on MRC documents could perhaps grant the MRC a level of significance that was unrepresentative of their actual role.

## 7.6 Future Directions

The limitations of my study design present opportunities for taking this research forward. For example, archival analysis of the other main funding bodies' documents regarding the origins and development of UK Biobank would not only be useful in gaining a wider understanding but it would counter the potential bias associated with analysing the MRC's documents only. It would be helpful to approach the Wellcome Trust, as the other main funding body, to seek permission again to access their material. By seeking access to the Department of Health's documents, one would also have the opportunity to analyse the role and involvement of government in the origins and development of UK Biobank, which would be a particularly useful extension of this research. Conducting follow-up interviews about the organisational changes with all interviewees in the main study would be a useful next step. If that could be done we would gain a greater understanding of the organisational changes and their effect.

As UK Biobank moves forward and recruitment nears completion, the opportunities for extending this research increase. For example, UK Biobank's greater public profile would allow an analysis of how it was presented in the media, be it the printed press or television. Detailed analysis of the format, headline, type of correspondent, language, tone, images and content would be particularly interesting. One could also undertake media analysis of in-house funding body publications (such as *Wellcome News*) and compare how the funding bodies portray UK Biobank, react to key events and how their approach to publicising UK Biobank compares to how they have previously published research initiatives. This analysis could be supplemented by interviews with the editors of in-house publications regarding their strategy in promoting UK Biobank. Widespread recruitment would also increase UK Biobank's profile amongst the wider academic scientific community considerably, which would foster awareness of the resource amongst academic scientists not involved in UK Biobank. One could therefore conduct further interviews with academic scientists indirectly involved as well as with those not involved in UK Biobank to balance the sample and access different perspectives. As UK Biobank continues to develop over the coming years it would also be useful to conduct follow-up interviews to monitor how perceptions of the resource change depending on its potential success or failure.



In conclusion, having originally intended to study lay and professional understandings and experiences of an ambitious large scale study of genetic and environmental influences on human health, I ended up studying the way in which this endeavour was initiated and originally organised. There were a number of delays in the implementation of UK Biobank which at least in part can be attributed to the organisational model (particularly hub and spokes) chosen. The simultaneous appointment of the hub, the spokes, and the CEO, and later appointment of the BoD; uncertainties about whether spokes would receive any privileged access to data and in what other ways they might benefit; the retirement of the original proponents early in the process; and the determining of the age range and sample size before the scientists who were to conduct the initiative were appointed; all contributed to initial difficulties in pushing UK Biobank forward. Data collection has just started as this thesis is submitted. It is to be hoped that the newer organisational arrangements will prove more effective than the earlier ones and that some lessons will have been learned about how to set up such large scale initiatives.

## **Appendix A: Chronology**

### **A1: Timeline**

#### **1998**

- |           |   |
|-----------|---|
| 29 May    | MRC post-genome challenge working group on DNA sample collections and facilities for large scale genetic typing           |
| July 1998 | MRC include proposal for a new large scale cohort study in their bid to the 1998 Government Comprehensive Spending Review |

#### **1999**

- |              |   |
|--------------|---|
| 14 May       | MRC/Wellcome Trust Workshop on UK Biobank |
| May          | EWG Established                           |
| 4 August     | First Meeting of EWG                      |
| 27 September | Second Meeting of EWG                     |
| 23 November  | Third Meeting of EWG                      |
| 4 December   | Fourth Meeting of EWG                     |

#### **2000**

- |       |                            |
|-------|----------------------------|
| March | EWG Final Report published |
|-------|----------------------------|

June MRC and Wellcome Trust agreed in principal to fund UK  
Biobank proposal

October ‘Public Perceptions of the Collection of Human Biological  
Samples’ report published by CraigRossDawson

## **2001**

January ‘Consultation with primary health care professionals on issues  
relating to the recruitment of patients to a DNA collection  
study’ report published by Genetics Interest Group and the  
Universities of Nottingham and Sheffield

17 April Protocol Development Workshop

May PDC Established

18 May First Meeting of PDC

21 June Second Meeting of PDC

25 July Third Meeting of PDC

26 September Consultation with Bio-Industries Association

19/20 October Fourth Meeting of PDC

October Draft Protocol and IPC Protocol completed

21 November Teleconference with CARTaGENE

27 November Teleconference with GlaxoSmithKline

17 December	Fifth Meeting of PDC
December	Draft protocol and IPC protocol sent to International Peer Review Panel and Ethical Review Panel
<b>2002</b>	
15 January	Meeting with Pfizer
22 February	Draft protocol and IPC protocol sent to MRC Council
27 March	MRC Council Funding Decision Meeting
March	MRC and Wellcome Trust decide to fund UK Biobank
	‘Biobank UK; A Question of Trust: A consultation exploring and addressing questions of public trust’ report published by People, Science and Policy (PSP)
25 April	Ethics Consultation Workshop
July	First meeting regarding the hub and spoke bidding process between representatives of the funding bodies and organisations interested in becoming the hub or a spoke
28 October	Expressions of interest sought for hub contract
30/31 October	Consultation with Industry Workshop at Hinxton Hall Conference Centre

13 November First round spoke bidders sent Pre-Qualification Questionnaire (PQQ)

19 November HGC Information Gathering Meeting

21 November Successful first-round spoke bidders notified

## **2003**

9 January Successful first-round hub bidders notified

January-February Site Visits for successful first-round hub bidders

14 February First Meeting of IAG

Spoke Selection Panel formed

25/26 February Second round spoke bidders met with funding bodies

17 March Successful spoke bidders notified

Successful hub bidder notified

March John Newton appointed as CEO of UK Biobank Limited

2/3 April Second Meeting of IAG

4 April Consultation with Industry Workshop at the Association of the British Pharmaceutical Industry (APBI)

7 April John Newton made his first appearance as CEO at a Parliamentary event

April	‘UK Biobank: A consultation with nurses in general practice and research’ report published by People, Science and Policy (PSP)
20 May	Meeting between representatives from the hub and spokes and representatives of the selection panel and the funding bodies
18 June	HGC Genetics sub-group Meeting
June	‘UK Biobank Consultation on the Ethical and Governance Framework’ report published by People, Science and Policy (PSP)
30 June/1 July	Third Meeting of IAG
23 July	Spoke Negotiating Team Meeting
July	Science Committee Established
August	‘Summary of the UK Biobank Consultation on the Ethics and Governance Framework’ report published by Opinion Leader Research
24 September	Draft of EGF published
10 October	Background document to EGF produced
28 November	UK Biobank incorporated as a private company limited by guarantee, UK Biobank Limited
30 December	UK Biobank Limited registered as a charity

**2004**

January	BoD Established
29 January	First meeting of BoD
	Joint Venture Agreement (JVA) completed between members of the company (Wellcome Trust as a trustee of the Wellcome Trust and the MRC) and UK Biobank Limited
26 March	Hub released pre-contract funding for the spokes
30 March	HGC Update Meeting
8 April	Draft hub and spoke contract circulated to spokes
30 April	Spokes responded to draft contract
November	EGC established
13 December	John Newton resigned as CEO of UK Biobank Limited

**2005**

17 January	Tim Peakman appointed as acting CEO
28 February	Phase One Pilot Study Commenced
8 August	Rory Collins appointed as CEO and PI
	Tim Peakman appointed Executive Director
August	Organisational Changes Commenced

## **A2: Committee members' biographies**

### **EGC**

#### **Professor Alastair Campbell (Chair)**

Alastair Campbell is the inaugural Professor of Ethics and the Director of the Centre for the Ethics in Medicine at the University of Bristol. He is a member of the Medical Ethics Committee of the British Medical Association and a member of the Wellcome Trust's Biomedical Ethics Funding Committee. Formerly, he was a member of the Chief Medical Officer's Expert Group on Cloning and Chairman of the Wellcome Trust's Standing Advisory Group on Ethics. He was also a member of the UK Biobank Interim Advisory Group (<http://www.egcukbiobank/org.uk/members/index.html> 2006) (accessed 14/02/06).

#### **Ms Andrea Cook OBE**

Andrea Cook is Chair of Water Voice Northumbria, which represents consumer interests in the water and sewerage industry. Formerly, she served as Chief Executive of the National Energy Action, a charity which promotes energy efficiency to address the problems of low-income consumers, a member of the UK Round Table on Sustainable Development and a member of the government's Advisory Group to the New Deal Task Force (<http://www.egcukbiobank/org.uk/members/index.html> 2006)(accessed 14/02/06).

#### **Ms Jayam Dalal**

Jayam Dalal is a freelance marketing consultant. She is a lay member on the Residential Property Tribunal Service (Public Appointment within the Office of the



Deputy Prime Minister), an Independent Assessor for Public Appointments within the Department of Culture, Media & Sport, a Partner within the Women's National Commission, a member of the Sussex Police's Independent Advisory Group and Domestic Violence Working Group  
(<http://www.egcukbiobank/org.uk/members/index.html> 2006)(accessed 14/02/06).

Professor the Baroness Finlay of Llandaff

Ilora Finlay is a consultant in palliative medicine and chronic pain at the Velindre NHS Trust, Cardiff. She is an Honorary Professor and Vice Dean of the University of Wales, College of Medicine and Director of the Institute of Medical Ethics. Formerly she served on many committees and advisory panels such as the Science Committee of Cancer Research UK and the Home Office Advisory Council on Misuse of Drugs Act. She was appointed a people's peer in 2001 in the first open contest for membership of the House of Lords  
(<http://www.egcukbiobank/org.uk/members/index.html> 2006)(accessed 14/02/06).

Professor Roger Higgs MBE

Roger Higgs is Professor Emeritus and former Deputy Head of division at GKT School of Medicine, King's College, London. In 2004 he retired from the Department of General Practice and Primary Care at King's. He chairs the Steering (Editorial) Committee of the Journal of Medical Ethics and sits on various committees for bioethics and healthcare organisations  
(<http://www.egcukbiobank/org.uk/members/index.html> 2006)(accessed 14/02/06).

Professor Ian Hughes

Ian Hughes is a Professor of Pharmacology at the School of Biomedical Sciences, University of Leeds. He is Chair of Leeds Mental Health NHS Teaching Trust and Vice-President (Academic Development) of the British Pharmacological Society and serves as a lay member of the General Osteopathic Council. Formerly, he held non-executive Director appointments in the NHS

(<http://www.egcukbiobank/org.uk/members/index.html> 2006) (accessed 14/02/06).

Ms Clara Mackay

Clara Mackay is Director for Policy and Research at Breast Cancer Care. She is Commissioner for the Patient and Public Involvement in Health Commission and Chair of the MRC/ESRC Innovative Health Technologies Research Programme Advisory Group. Formerly, she was Principal Policy Adviser (Health) for the Consumers' Association and a member of the Public Advisory Group to the NHS National IT Programme - Electronic Records

(<http://www.egcukbiobank/org.uk/members/index.html> 2006) (accessed 14/02/06).

Professor Sheila McLean

Sheila McLean is the first holder of the International Bar Association Chair of Law and Ethics in Medicine at Glasgow University and Director of the Institute of Law and Ethics in Medicine at Glasgow University. She is a member of the Wellcome Trust's Biomedical Ethics Funding Committee. Formerly, she was a consultant to the World Health Organisation and the Council of Europe, and to individual States, chaired the Scottish Independent Review Group on Retention of Organs at Post-Mortem, the Scottish Criminal Cases Review Commission, and the Scottish Office Steering Group on Female Offending. She was appointed by the Department of

Health to review the Consent Provisions of the Human Fertilisation and Embryology Authority (<http://www.egcukbiobank/org.uk/members/index.html> 2006) (accessed 14/02/06).

#### Ms Sally Smith QC

Sally Smith is a practising Barrister and was appointed Queen's Counsel in 1997, specialising in medical law. She is a member of the Royal College of Physicians Ethics Committee and the MRC ethics committee. Formerly, she was a member of the St Thomas' Hospital Research Ethics Committee. She has represented the NHS in major litigation including the Benzodiazapine Litigation, the Breast Radiation Litigation and the Nationwide Organ Retention Litigation (<http://www.egcukbiobank/org.uk/members/index.html> 2006) (accessed 14/02/06).

#### Professor Sandy Thomas

Sandy Thomas is the Director of the Nuffield Council on Bioethics and a Professor within the Science Policy Research Unit (SPRU) at the University of Sussex. She is a member of the Royal Society's Science and Society Committee, the Genetics Society, the Editorial Board for Science and Public Affairs and the Academy of Medical Sciences Working Group: Impediments to Medical Research (<http://www.egcukbiobank/org.uk/members/index.html> 2006) (accessed 14/02/06).

#### Professor Christopher Wild

Chris Wild is Professor of Molecular Epidemiology and Head of the Centre for Epidemiology and Biostatistics at the University of Leeds. He serves as Chair of the UK Molecular Epidemiology Group and is Senior Editor on the Cancer

Epidemiology, Biomarkers and Prevention journal. Formerly he was Chief of the Unit of Environmental carcinogenesis at the International Agency for Research on Cancer in Lyon, France (<http://www.egcukbiobank/org.uk/members/index.html> 2006) (accessed 14/02/06).

### **Science Committee**

Professor John Bell (chair)

John Bell is Regius Professor of Clinical Medicine at the University of Oxford. He is a Member of Council of the University of Oxford and a Trustee of The Rhodes Trust. Formerly, he served as Nuffield professor of clinical medicine, University of Oxford, held a clinical fellowship at Stanford University, California and co-founded the Wellcome Trust Centre for Human Genetics in Oxford (<http://www.ukbiobank.ac.uk/science/sciencecomm> 2006) (accessed 14/02/06).

Professor Valerie Beral

Valerie Beral is Professor of Epidemiology at the University of Oxford and Director of the Cancer Research UK epidemiology unit, Oxford. She is the Principal Investigator of the Million Women Study, fellow of the Royal College of Physicians and an honorary fellow of the Academy of Medical Sciences, the Faculty of Public Health Medicine and the Royal College of Obstetricians and Gynaecologists. She is Chair of the Department of Health's Advisory Committee on Breast Cancer Screening. Formerly, she was a member of the Health Services and Public Health Board and the Physiological and Infections Board of the Medical Research Council and served on international committees for the World Health Organisation and the

National Academy of Sciences, USA

(<http://www.ukbiobank.ac.uk/science/sciencecomm> 2006) (accessed 14/02/06).

Professor Paul Burton

Paul Burton is Professor of Genetic Epidemiology and Head of the Genetic Epidemiology Unit at the University of Leicester. He is a chartered statistician (Royal Statistical Society), a member of the Royal College of Physicians (UK), and of the Faculties of Public Health Medicine both in the UK and Australia. Previously, he was senior biostatistician and head of the division of biostatistics at the Institute for Child Health Research, Perth, Western Australia

(<http://www.ukbiobank.ac.uk/science/sciencecomm> 2006) (accessed 14/02/06).

Professor John Danesh

John Danesh is Professor of Epidemiology and Medicine and Head of the Department of Public Health and Primary Care and Honorary Co-Director of the Strangeways Research Laboratory at the University of Cambridge

(<http://www.ukbiobank.ac.uk/science/sciencecomm> 2006) (accessed 14/02/06).

Professor Paul Elliott

Paul Elliott is Professor of Epidemiology and Public Health Medicine and Head of the Division of Primary Care and Population Health Sciences in Imperial College London. He is a fellow of the Academy of Medical Sciences. Formerly, he was Head of the Environmental Epidemiology Unit at the London School of Hygiene and Tropical Medicine and Head of the WHO Collaborating Centre in Environmental Epidemiology. He was a specialist adviser to the House of Lords Science and

Technology Sub-Committee on Human Genetic Databases (2000-2001)

(<http://www.ukbiobank.ac.uk/science/sciencecomm> 2006) (accessed 14/02/06).

Professor Hilary Graham

Hilary Graham is Professor of Social Policy at Lancaster University. She is a member of the NHS Advisory Committee on Research Allocation (ACRA) and of the new Department of Health Inequalities Scientific Research Group. Formerly, she directed the ESRC Health Variations Programme, was a member of the Independent Inquiry into Inequalities in Health (Acheson Report) and served on the MRC Health Services and Public Health Research Board

(<http://www.ukbiobank.ac.uk/science/sciencecomm> 2006) (accessed 14/02/06).

Bernard Keavney

Bernard Keavney is Professor of Cardiology at the University of Newcastle and consultant cardiologist to the Newcastle upon Tyne Hospitals NHS Trust. Formerly, he was an MRC Training Fellow at the Wellcome Trust Centre for Human Genetics and clinical lecturer in cardiology at Oxford

(<http://www.ukbiobank.ac.uk/science/sciencecomm> 2006) (accessed 14/02/06).

Professor John Newton

John Newton was the CEO of UK Biobank from April 2003 until December 2004. Formerly, he was consultant epidemiologist for the Unit of Health Care Epidemiology, Department of Public Health and Primary Care at the University of Oxford and the Oxford Radcliffe Hospitals NHS Trust. He was also Director of Research and Development at the Oxford Radcliffe NHS Trust and Head of a research

team supporting the Government's national Clinical Standards Advisory Group (<http://www.ukbiobank.ac.uk/science/sciencecomm> 2006) (accessed 14/02/06).

#### Professor Stephen Palmer

Stephen Palmer is the Mansel Talbot Professor of Epidemiology and Public Health at the University of Wales College of Medicine and Director of the Health Protection Agency's division of chemical hazards and poisons. Formerly, he was Head of the Communicable Disease Surveillance Centre (Wales), served on the MRC Health Services and Public Health Research Board and was a member of the Advisory Committee on the Microbiological Safety of Food (<http://www.ukbiobank.ac.uk/science/sciencecomm> 2006) (accessed 14/02/06).

#### Professor Catherine Peckham

Catherine Peckham is Professor of Paediatric Epidemiology, Institute of Child Health, University College London. She chairs the Medical Research Council/Human Fertilisation and Embryology Authority Working Group on assisted reproduction, the MRC/MoD Military Health Advisory Group, the Confidential Enquiries Advisory Committee, National Institute for Clinical Excellence and vice-chair of the Nuffield Council on Bioethics. She is a member of the Wellcome Trust Biological Collections Advisory Committee and Board of Management of the Centre for Longitudinal Studies, Institute of Education. Formerly, she founded and was head of the Centre for Paediatric Epidemiology and Biostatistics at the Institute of Child Health, established the Department of Community Medicine and General Practice, Charing Cross Hospital Medical School. She was also founder fellow of the Academy of Medical Sciences, non-executive Director of the Advertising Standards Authority and a

Fulbright Commissioner (<http://www.ukbiobank.ac.uk/science/sciencecomm> 2006) (accessed 14/02/06).

#### Professor Jill Pell

Jill Pell is a consultant in Public Health at Greater Glasgow NHS Board and an honorary reader in the Division of Cardiovascular Medicine and Sciences at the University of Glasgow. She is a member of the Royal College of Physicians (Edinburgh) Audit and Research Committee, the Chief Scientist Office Biomedical and Therapeutic Research Committee and she is the lead of the Scottish RCC. Formerly, she sat on committees and working groups established by Quality Improvement Scotland and the Scottish Intercollegiate Guidelines Network and established a Scotland-wide register of adult cardiac surgery and a Scotland-wide register of percutaneous coronary interventions (<http://www.ukbiobank.ac.uk/science/sciencecomm> 2006) (accessed 14/02/06).

#### Professor Mike Pringle

Mike Pringle is the Professor of General Practice and Head of the School of Community Health Sciences in the University of Nottingham. He is Strategic director of PRIMIS, which is a service contracted by the NHS Information Authority to improve the use of computers and data in primary care. He was elected to the General Medical Council for 3 years from July 2003 and sits on the Council of the Medical Defence Union. Previously, he was Chairman of the Council of the Royal College of General Practitioners and co-chair of the External Reference Group and the Implementation Group for the National Service Framework for diabetes (<http://www.ukbiobank.ac.uk/science/sciencecomm> 2006) (accessed 14/02/06).



### Professor Alan Silman

Alan Silman is Director of the UK Arthritis Research Campaign Epidemiology Unit, University of Manchester Medical School, Professor of Rheumatic Diseases Epidemiology and Consultant in Rheumatology in Manchester. He is the senior author of *Epidemiology of the Rheumatic Diseases* and one of the five new editors of the third edition of the rheumatology textbook *Rheumatology* (<http://www.ukbiobank.ac.uk/science/sciencecomm> 2006) (accessed 14/02/06).

### Professor John Todd

John Todd is Professor of Medical Genetics at Cambridge University in the Cambridge Institute for Medical Research. He is director of the Diabetes and Inflammation Laboratory at Cambridge University. He is scientific adviser for several companies including Amersham and Unilever. Previously, he was Professor of Human genetics at Oxford University and Wellcome Trust Principal Research Fellow (<http://www.ukbiobank.ac.uk/science/sciencecomm> 2006) (accessed 14/02/06).

### Madeline Wang

Madeline Wang is a board member of the Northern and Yorkshire Clinical Trials Unit and lay-member of the General Optical Council, the MRC/Wellcome Trust Joint Steering Committee on Human Developmental Biological Resources, the Northern and Yorkshire Multi-centre Research Ethics Committee and the Royal College of Anaesthetists. Formerly, she was an NHS Trust Chair and Trustee of the National Childbirth Trust and a member of the MRC Working Group on Personal Information in Medical Research and worked as a nursing auxiliary and as a student nurse in a wide variety of NHS hospital settings, both acute and chronic, and with a range of

patient groups (<http://www.ukbiobank.ac.uk/science/sciencecomm> 2006) (accessed 14/02/06).

## **BoD**

Sir Alan Langlands (Chair)

Alan Langlands is the Principal and Vice Chancellor of the University of Dundee and Chairman of the Scottish Institute for Enterprise. He is a Fellow of the Royal Society of Edinburgh and an Honorary Professor at the University of Warwick Business School. He is a member of advisory boards at INSEAD, the Johns Hopkins University Bioethics Institute, chairs the development board of IVIMEDS (the International Virtual Medical School) and Convener of the Universities Scotland Funding Policy Group. He was awarded honorary fellowships by four medical Royal Colleges and the Institute of Actuaries and received a knighthood in the Queen's Birthday Honours List (1998) for services to the NHS. Formerly, he was the Chief Executive of the NHS in England and accountable to Parliament for a £42bn revenue budget (<http://www.ukbiobank.ac.uk/about/board> 2004) (accessed 14/09/04).

Professor John Bell-see above

The Hon Peter Benson LVO

The Hon Peter Benson LVO is a non-executive Director for a number of commercial and charitable concerns. He was a senior partner in PricewaterhouseCoopers retiring in 2001 and had a significant role in the privatisation of British Telecom, specialising in this area and lecturing in various parts of the world on privatisation and other

financial topics, frequently on Government and Ministerial Missions

(<http://www.ukbiobank.ac.uk/about/board> 2004) (accessed 14/09/04).

#### Professor David Gordon

David Gordon studied at Cambridge and the Westminster Medical School, qualifying in 1970. His early professional training was in Cambridge and in Leicester, and he then worked in research and academic posts at St. Mary's Hospital Medical School from 1972 to 1983. In 1983 he moved to the Wellcome Trust, while maintaining a clinical commitment at St Mary's Hospital. Professor Gordon's work at the Wellcome Trust involved him in a wide range of activities concerned with the funding of science. Professor Gordon took up his appointment as Dean of the Faculty of Medicine, Dentistry, Nursing and Pharmacy, and Professor of Medicine, in the University of Manchester, on 1 September, 1999. He is Fellow of the Academy of Medical Sciences, Chair of the Council of Heads of Medical Schools, Vice-President of the Association of Medical Schools in Europe, and a member of a number of national scientific and professional advisory bodies

(<http://www.ukbiobank.ac.uk/about/board> 2004) (accessed 14/09/04).

#### Ms Jane Lee

Jane Lee is Director of Corporate Affairs at the Medical Research Council. She is one of the UK members of the Board of Trustees for the Human Frontier Science Program in Strasbourg and a non-executive member of the Board of MVM Limited (which creates finances and builds life science companies from MRC and other academic research). Formerly, she managed the initial introduction of formal performance appraisal for scientific staff in human resources group, the MRC's earliest ventures in

working with the biotech industry in technology transfer and the Council's global health portfolio in research management group

(<http://www.ukbiobank.ac.uk/about/board> 2004) (accessed 14/09/04).

Professor Mike Pringle-see above

Dr Barbara Skene

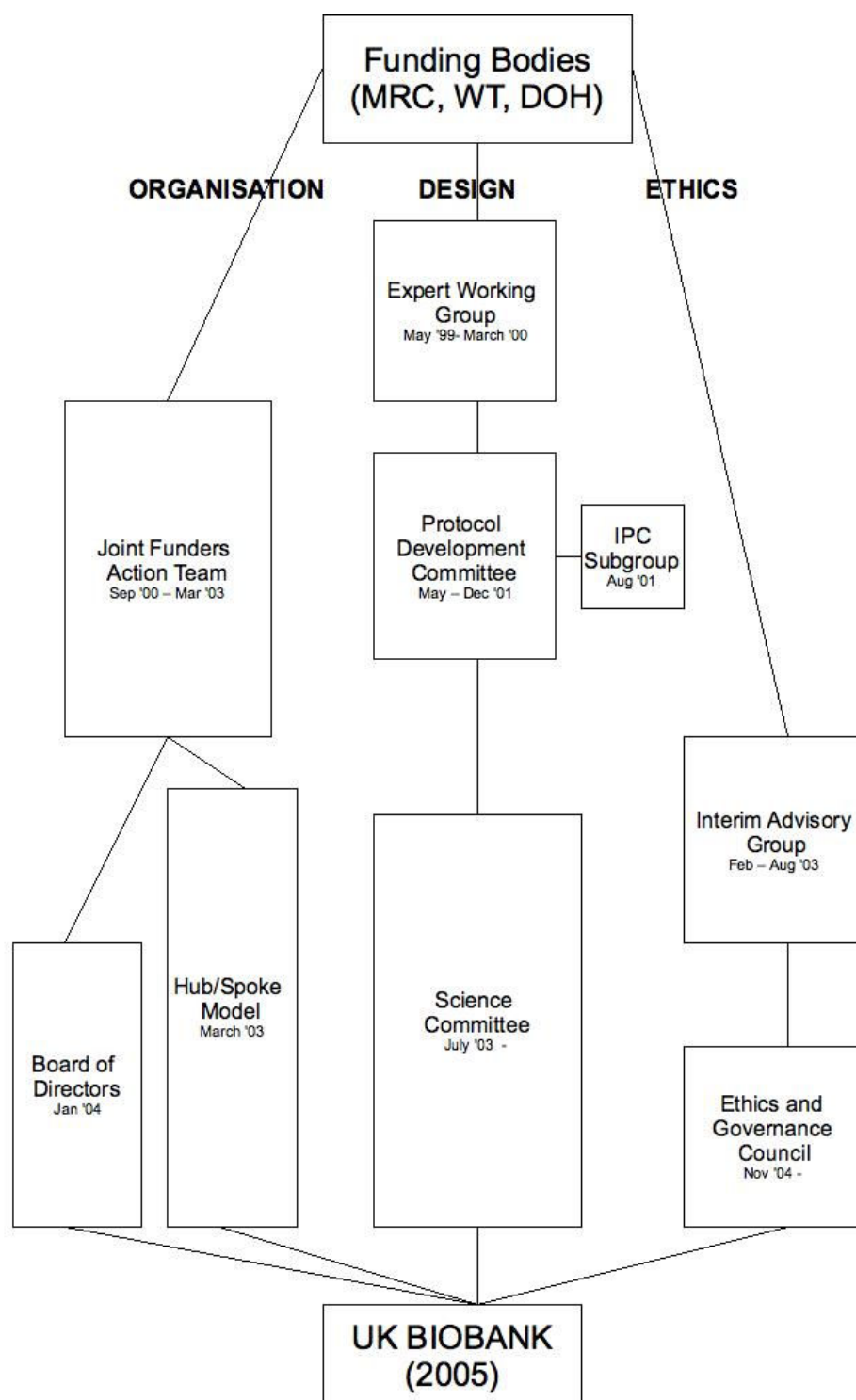
Barbara Skene is Head of Department Ventures and Initiatives at the Wellcome Trust. She is also a Director on the Board of the Structural Genomics Consortium. Formerly, she was a scientific administrative officer at the MRC. She was appointed to the scientific staff of the Wellcome Trust in 1993 as secretary to the genetics Advisory Group and became deputy chairman of the group in 1996

(<http://www.ukbiobank.ac.uk/about/board> 2004) (accessed 14/09/04).

Mr Marc Taylor

Marc Taylor is Head of Research Policy in the Research and Development Directorate of the Department of Health. Formerly, he was head of NHS R&D Policy when his responsibilities included management of the £550m national NHS R&D Budget. He was head of estate policy and director of finance at NHS Estates, served in the Foreign and Commonwealth Office and was Head of the development section at the British High Commission in India. Marc Taylor replaced Dr Peter Greenaway who retired from the Department of Health in 2004

(<http://www.ukbiobank.ac.uk/about/board> 2004) (accessed 14/09/04).

**A3: Organisational Diagram**

## Appendix B: Methods

### **B1: Invitation Letter**

[MRC logo]

#### A contemporary history of UK Biobank

Dear ...,

I am undertaking a PhD on the contemporary history of the UK Biobank and I am writing to ask whether you would be willing to be interviewed. I began this MRC funded studentship in October 2003 and am supervised by Sally Macintyre and Kate Hunt from the MRC Social and Public Health Sciences Unit. The aim of my project is to document the origins, implementation and evolution of the UK Biobank in its historical and international context, primarily using oral history techniques. The overall research question is: how and why has UK Biobank been set up at this particular time and in this particular way?

I am approaching a range of people both directly and indirectly involved in the UK Biobank. I enclose an information sheet about the project and a consent form, which I would invite you to sign should you agree to be interviewed. If you agree to take part, the interview will be conducted in a place of your choosing, such as your office, at a time that best suits you. It should last about an hour. I would ask you about your involvement, experiences and opinions of the UK Biobank. Although I would prefer to conduct interviews face to face, if you are unable to do so I could carry out telephone interviews lasting half an hour. Ideally I would record the interview so that I can concentrate on our conversation and have an accurate record of it, but if you would prefer it not to be recorded I would take notes.

I appreciate that you are a very busy person, but I would very much value the opportunity to speak with you, since I believe you would make an important contribution to this project.

Please let me know by email, phone, fax or post whether or not you would consider being interviewed.

Thank you for your time.

Yours sincerely

Mairi Langan  
Direct Line: 0141 357 7545  
E-mail: [mairi@msoc.mrc.gla.ac.uk](mailto:mairi@msoc.mrc.gla.ac.uk)

[MRC Social and Public Health Sciences Unit Contact Information]

## **B2: Information Sheet**

### A contemporary history of UK Biobank

#### PhD research project

#### Information Sheet

#### Introduction

As the world's largest genetics database, examining the role of genetic, lifestyle and medical factors in disease, the UK Biobank promises to be a high profile and influential research endeavour. The international context of this type of research adds a further dimension to its significance.

#### Nature of the research project

This research project is a contemporary history and will primarily use in-depth face to face or telephone interviews to elicit the experiences and opinions of scientists and interest groups regarding the evolution of the UK Biobank. It will also involve analysis of archival material on UK Biobank.

#### Aims

The main aims of this research project are to understand:

- The origins, implementation and evolution of the UK Biobank in its historical and international context.
- How and why was UK Biobank set up when it was and how it was?

#### Why is your participation important?

This project offers an opportunity to understand how such an important scientific study developed from conception into operation. To achieve these aims I will speak to leading scientists, funders and interest groups directly and indirectly involved in the UK Biobank. Such first-hand accounts are crucial in gaining an understanding of the origins of the UK Biobank.

#### What would taking part involve?

Participation in this study involves an interview lasting about an hour. The interview will be held at a time and place of your choosing and it will be arranged so as to cause you the least inconvenience. If you are unable to be interviewed face to face, a telephone interview lasting around half an hour can be arranged instead. If you agree to be interviewed, please contact me and I will make the arrangements.

#### What topics will be discussed?

During the interview you will be asked about your involvement, experiences and opinions regarding the origins, implementation and evolution of the UK Biobank.

#### Ethical issues

This research project has received the approval of the Ethics Committee of the University of Glasgow's Faculties of Law and Financial Studies and Social Sciences. Two key ethical issues are consent and confidentiality.

### Consent

Your consent will be obtained for the interview to be carried out, for it to be tape-recorded with permission, and for the use of the transcript. You will be able to withdraw from the study at any point during the interview, or to decline to answer any questions that you are uncomfortable with. If you have any questions regarding the study I would be happy to try to answer them. It would be very useful to me if I could tape record the interview but if you are uncomfortable with this then I can simply take notes.

### Confidentiality

Only my supervisors and myself will have full access to the recordings and transcripts generated during this study. If the recording is transcribed by a professional typist she/he will be bound by the MRC 'Good Research Practice' guidelines, and I will remove any identifying information. In order to protect your confidentiality your name, contact details and job title will be stored in hard copy only and will be kept in a locked cabinet separate from recordings and transcripts. The data would be suitably anonymised by mutual agreement; a general descriptor would be used e.g. 'member of a spoke', 'member of a funding organisation' and a general professional descriptor would also be used e.g. 'general practitioner', 'geneticist' 'epidemiologist'.

Please contact me by post, phone, fax or email:

Write to: Mairi Langan, MRC Social and Public Health Sciences Unit, University of Glasgow, 4 Lilybank Gardens, Glasgow G12 8RZ.

Telephone: 0141 357 7545

Fax: 0141 337 2389

Email: [mairi@msoc.mrc.gla.ac.uk](mailto:mairi@msoc.mrc.gla.ac.uk)



**B3: Consent Form 1**

A contemporary history of UK Biobank

PhD research project

Consent Form – Part One

**Section A**

- I understand the nature of the research project as described in the information sheet and I am willing to be interviewed.
- I understand that I can decline to answer any question and that I can withdraw from the interview at any point.

Name

Signature

Date

**Section B**

Please select one of the following options:

- I agree that this interview can be tape recorded
- I do not wish this interview to be tape recorded

Signature

Date

**B4: Consent Form 2**A contemporary history of UK BiobankPhD research projectConsent Form – Part Two

In concordance with copyright laws, you are the owner of the copyright in the words and the MRC Social and Public Health Sciences Unit is the owner of the copyright in the recording. In order to consult the interview and to use the transcript in research, the copyright in the words must be transferred from you to me by signing this form.

## Section A

Please choose one of the following options:

- I hereby grant the researcher permission to use extracts or quotations from the transcript for the purposes of the PhD thesis or any subsequent publications in suitably anonymised form by a general descriptor e.g. ‘member of the protocol development committee’, ‘member of a spoke’. Also, to distinguish the discipline I grant the researcher permission to refer to my speciality e.g. ‘sociologist’, ‘primary care’, ‘epidemiologist’.
- I hereby grant the researcher permission to use extracts or quotations from the transcript for the purposes of the PhD thesis or any subsequent publications in identifiable form e.g. by name (if wished) and I also grant the researcher permission to refer to my speciality e.g. ‘sociologist’, ‘primary care’, ‘epidemiologist’.

Name

Signature

Date

## Section B

You may wish to check the transcript for any factual errors or to make any further observations.

Please choose one of the following options

- I would like to see the transcript
- I would not like to see the transcript

Signature

Date

**B5: Transcript Return Letter**

[MRC Logo]

## A contemporary history of UK Biobank

Dear ...,

I would like to take this opportunity to thank you once again for the interview. I appreciate how busy you must be and I am very grateful for the time that you gave me. I have enclosed a copy of the transcript and would invite you to check it for any factual errors and misspellings and also, if you wish, to make any additions or clarifications. If you would like to make any corrections or amendments to the transcript I would be very thankful if you would return it to me within three months. I would also like to take this opportunity to explain the changes that I have made to the transcript and provide some clarification on how I may use the information.

I have put any identifying information in square brackets. If I were to use the quotation surrounding the bracketed information then I would change the contents of the square brackets into something less identifiable, for example 'place of work'. Therefore, the information in the square brackets is data that I would have to change if I were to use the quotation.

If I were to use any quotations from the transcript then I would refer to your position as 'member of a Spoke' / 'member of the Science Committee' / 'member of the Ethics and Governance Council' / 'member of the Board of Directors' / 'member of the Protocol Development Committee' and where appropriate as an 'general practitioner' / 'epidemiologist' / 'sociologist' as it might be useful to make the distinction in discipline between individuals (whether or not directly involved in the UK Biobank). I will not make any distinction between members of and leads or chairs of spokes/committees/boards. I am trying to interview several members of each spoke and multiple members of each committee (as well as a lot of people who are not members of spokes or committees); this will further serve to protect your identity.

If I were to use quotations from your interview then it would be to illustrate a general point and usually as part of several quotations from different people to support that point. For example, a theme might be the funding of the project and a finding might be that some people thought that the figure was not high enough, whereas others thought it was adequate. In this case I would perhaps write, 'several people involved with UK Biobank thought that the figure was not high enough whereas others involved thought it was fine, and comments included...' I would then use several quotations from each perspective as illustrative of this point.

Thanks again for your help and do not hesitate to contact me should you have any questions or queries,

Mairi Langan  
Direct Line: 0141 357 7545  
E-mail: mairi@msoc.mrc.gla.ac.uk

[MRC Social and Public Health Sciences Unit Contact Information]

## **B6: Interview Schedule**

### A contemporary history of UK Biobank

#### Topic Guide

#### Key Objectives

To document the origins, development and implementation of UK Biobank in its historical and international context

How and why was UK Biobank set up when it was and how it was?

#### Origins

##### Experience

How did you first become aware of the initial idea for UK Biobank?

When did you first become aware of the idea?

How did you first become involved in it?

Are you still involved in UK Biobank?

What did you think about the initial idea for UK Biobank at the time?

##### Initial Idea

Where did the initial idea for UK Biobank come from?

When was the idea first put about?

Why do you think it emerged then?

Who or what groups first thought of it?

What were the initial reactions to it from the scientific community?

#### Implementation

##### Establishment

What do you think about the way that the project has been set-up and managed?

Why do you think it has been established the way it has?

##### Key players

Who and what drove the study?

##### Timing

Why do you think it came about when it did?

What were the factors that allowed the UK Biobank to emerge when it did?

What do you think about the project's timescale?

##### Funding

What do you think about the involvement of the funding bodies?

When did each of the organisations become involved?

How did they become involved?  
How do you view the relationship between them?

What do you think about the amount of money committed to funding the study?

### Evolution

#### Funder's role

Other than to provide the financial support for the project, what do you see as the role of the funders in the project generally?  
What do you think about the role that the funders have had?

#### Scientific Protocol

What do you think about the way in which the initial protocol was formed?

What did you think about the initial scientific protocol?  
What did you think about the key decisions taken?  
Do you feel that all the opportunities were taken or do you feel that some opportunities were missed in regard to the protocol?

#### Organisational Structure

What did you think about the organisational structure for UK Biobank? ('hub/spoke' model, national/collaborative effort, the decision to set up Biobank Limited)

Why do you think these organisational structures were chosen? ('hub/spoke' model, setting up of Biobank Limited)

#### As a spoke member

What motivated you to apply to be a spoke?

What was your experience of the bidding process for the spoke contracts?  
How did you feel when you were selected to be a spoke?

What has been your experience of being a spoke?  
What has been the key issues in your experience of being a spoke?

Upon becoming a spoke, how do you feel your group has influenced the development of UK Biobank in this capacity?  
In your capacity as spoke member, how do you feel you have influenced the development of UK Biobank?

#### Personal Involvement

What motivated you to becoming involved in UK Biobank?

#### Future Interviewees

With regard to the origins and development of the study, who or what types of people would you recommend that I interview in the future?

#### International Context

What do you think about the international context of similar concepts?

How do you think the UK Biobank compares to international studies and proposals?

Why do you think that this study was set up in the UK?

**B7: Follow-up Interview Schedule**Follow-up Interview Topic GuideChanges to the Organisational Structure of UK Biobank

What is your understanding of the new organisational structure?

When was this new model introduced?

How was it introduced?

What do you think about the new organisational structure?

What are its pros and cons?

What has been your experience, thus far, of working within it?

What are the implications for UK Biobank of implementing of this new organisational structure?

Are there any issues that it might solve or bring?

Why was the organisational structure changed?

Who or what groups were responsible for the changes?

Why was the new approach adopted for as opposed to other options?

How does the new structure compare with the previous 'hub' and 'spoke' model?

What were the pros and cons of the previous 'hub' and 'spoke' model?

What do you think about the way in which the structure has developed?

What has been your experience of the process of implementing a different structure?

## **B8: Archival Research Information Sheet and Conduct Agreement**

### **A contemporary history of UK Biobank**

#### **PhD Research Project**

The following is a document that outlines the nature of my research project and details how I plan to use the MRC documents on the UK Biobank.

#### **Nature of the research project**

This research project is a contemporary history and will primarily use in-depth face to face or telephone interviews to elicit the experiences and opinions of scientists and interest groups regarding the evolution of the UK Biobank. It will also include analysis of archival material on UK Biobank. I aim to interview a range of scientists, funders and interest groups directly involved in the UK Biobank (such as key stakeholders, committee members) and indirectly involved (such as unsuccessful bidders, critics).

The main aims of this research project are to understand:

- The origins, implementation and evolution of the UK Biobank in its historical and international context.
- How and why UK Biobank was set up when it was and how it was.

#### **Purpose of archival analysis**

I hope to use the material available in the MRC documents to build up a clear picture of what took place during the early stages of the project, the main issues faced and the key people involved. I do not intend to use the material to report personal issues or opinions. I am fully aware of the sensitivity of the material and the importance of protecting people's identities.

#### **Handling of the material**

- I intend to use my laptop computer to log the general content of the documents such as reference number, name, date, topic area, name of the people involved and any further information regarding its contents if necessary.



- Although I will record the names of the people involved in my notes they will not appear in any written work and will instead be referred to by a suitably anonymous general descriptor.
- Similarly, the anonymity of all reviewers will be preserved. I will not report directly on who said what but will instead use the comments for my own understanding and interpretation of the information.
- Due to the sensitive nature of the material I will not photocopy any of the documents but will instead take notes from them at the MRC Headquarters thus ensuring that the documents are not removed from the building in any form whatsoever.
- I agree to maintain the same working hours as the individual responsible for the documents.

I am very grateful for the access I have been given to these important documents and the help I have been given in accessing them. I undertake to use the documents in a responsible manner and behave in an appropriate way regarding them as detailed above.

Please do not hesitate to contact me if you have any queries regarding my research.

Mairi Langan

MRC Social and Public Health Sciences Unit  
University of Glasgow  
4 Lilybank Gardens  
Glasgow  
G12 8RZ  
Telephone: 0141 357 7545  
Email: [mairi@msoc.mrc.ac.uk](mailto:mairi@msoc.mrc.ac.uk)

**B9: List of Transcripts**Members of the IAG

090

091

Members of the PDC

024

033

051

Members of the EWG

060

061

062

Members of the EGC

090

0400

0401

Members of the Science Committee

012

Members of the BoD

013

070

Spoke Members

021

022

023

025

026

027

030

035

052

080

0101

0102

0103

0104

0105

0200

0201

0202

0203

0204

0302  
0501  
0502  
0503  
0800

Clinical academic involved in UK Biobank  
071

Members of the scientific community outwith UK Biobank  
0700  
0900

Representatives of the Funding Bodies  
040  
041  
042  
043  
044  
063  
072

Representatives of UK Biobank Limited  
010  
0600  
0602

### **Follow-Up Interview Transcripts**

Spoke Members  
E2000  
E2001  
E2002  
E2004  
E2005  
E2007  
E2009

Clinical academic involved in UK Biobank  
E2010

Representatives of the Funding Bodies

E2003

E2008

E2011

Representatives of UK Biobank Limited

E2006

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